



MEHLMANMEDICAL
HY INTERNAL MEDICINE



YouTube
@mehlmanmedical



Instagram
@mehlman_medical

HY Internal Medicine – by Dr Michael D Mehlman

Table of Contents

IM Cardio	4
IM Pulmonary	40
IM Renal	77
IM Gastro	103
IM Heme/Onc	149
IM Repro/Obgyn	180
IM Derm	212
IM Neuro	241
IM Psych	279
IM Ophthal	293
IM MSK	308
IM Immuno	332
IM Biochem	336
IM Gen Path	338
IM Endocrine	347
IM mixed bullet points	375

IM Cardio

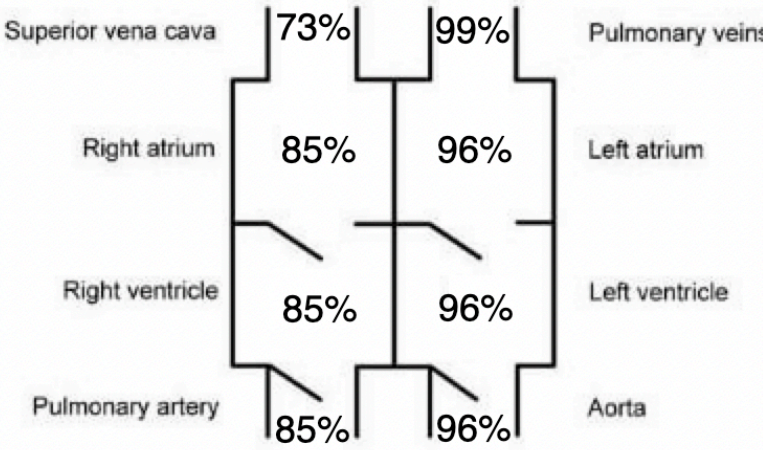
Important basic heart failure points	
Left heart failure	<ul style="list-style-type: none"> - Presents as pulmonary findings (i.e., dyspnea, orthopnea, paroxysmal nocturnal dyspnea). - This is because left-heart problems cause a backup of pressure onto the pulmonary circulation, leading to increased pulmonary capillary hydrostatic pressure → transudation of fluid into the alveolar spaces (pulmonary edema). Sometimes this can also cause pleural effusion. - Left atrial pressure (LAP) = pulmonary capillary wedge pressure (PCWP). - Therefore, if there is left heart pathology, PCWP is high (exceedingly HY). - Conversely, if a Q gives you normal PCWP, you know there's nothing wrong with the left heart. Qs will often give high PCWP and low BP, where you need to know immediately that means cardiogenic shock. - What USMLE will do is give you some sort of left-heart pathology + dyspnea, and then ask for the cause of the dyspnea → answer = "increased pulmonary capillary hydrostatic pressure." Another answer in this case is "increased alveolar-arteriolar (A-a) oxygen gradient."
Right heart failure	<ul style="list-style-type: none"> - Presents as systemic findings – i.e., jugular venous distension (JVD) and peripheral edema. - Since blood cannot enter the right heart as easily, it backs up to the neck veins (JVD) and venous circulation (increased hydrostatic pressure in veins → transudation of fluid into legs). The Q might mention that central venous pressure is high. - Hepatosplenomegaly can also be seen in RHF but is very rare on USMLE. - Normal jugular venous pressure (JVP) is 3cm above the sternal angle. JVD would be higher than this. Sometimes questions can write that jugular venous pulsations are seen 3cm above the sternal angle and the student erroneously thinks this means JVD, but this is not the case.
Congestive heart failure	<ul style="list-style-type: none"> - Congestive heart failure = left heart failure + right heart failure. - The most common cause of right heart failure is left heart failure. Simply adding the two together, we now call that congestive heart failure. - In congestive heart failure, we'll see both left- and right-heart failure findings – i.e., patient will have dyspnea, JVD, and peripheral edema. - PCWP is elevated in these patients, since the left heart has pathology.
Cor pulmonale	<ul style="list-style-type: none"> - Cor pulmonale is defined as right-heart failure due to a pulmonary cause. In other words, the left heart is completely normal in cor pulmonale and PCWP is normal. - Cor pulmonale will be a patient who has JVD and peripheral edema in the setting of obvious and overt lung disease, such as 100-pack-year smoking history, cystic fibrosis, or pulmonary fibrosis. These can present with lung findings such as wheezes, where you as the student need to say, "It just doesn't seem like they're focusing on left-heart failure as the cause of the right-heart failure here. It seems the 100-pack-year smoking Hx causing COPD is why the right heart is failing." - The patient can have a "boot-shaped" heart colloquially, which refers to right ventricular hypertrophy without left ventricular hypertrophy. - If the patient has COPD, the massively hyperinflated lungs will push the heart to the midline, causing a long, narrow cardiac silhouette, with a point of maximal impulse in the sub-xiphoid space. - You must know that <i>pulmonary hypertension</i> is the reason the right heart decompensates. In both cor pulmonale and congestive heart failure, the right heart experiences increased afterload because of <i>pulmonary hypertension</i>.

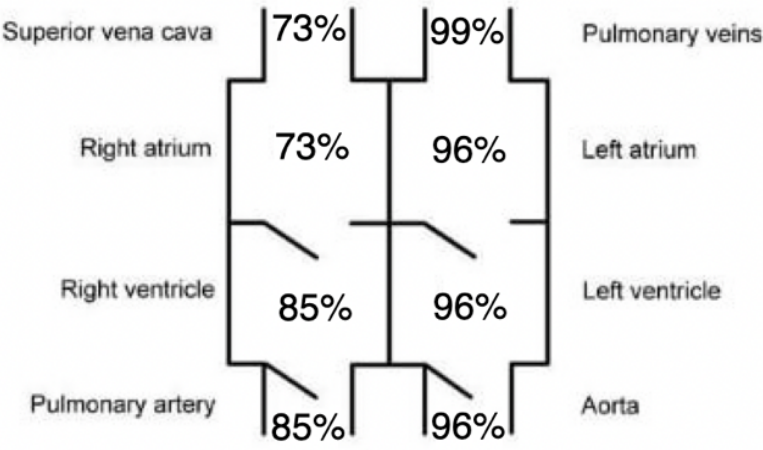
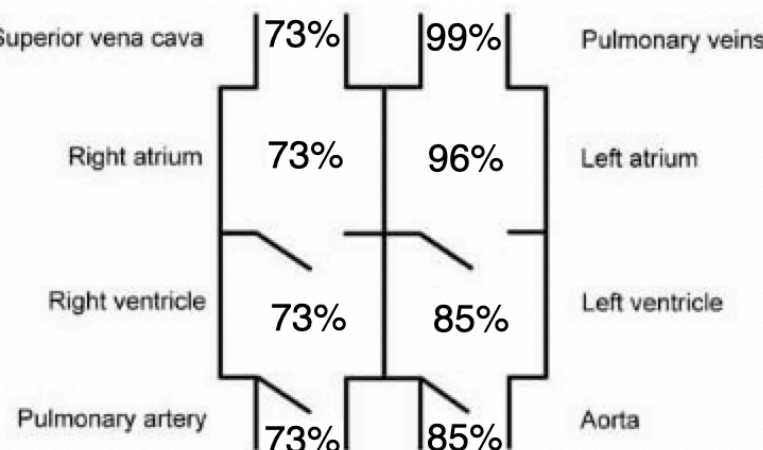
	<ul style="list-style-type: none"> - Endothelin 1 is vasoconstrictor and key mediator in pulmonary hypertension. USMLE wants you to know this is increased in both cor pulmonale and left heart failure. Bosentan is an endothelin 1 receptor antagonist. - Nitric oxide synthase, in contrast, USMLE wants you to know is decreased in pulmonary hypertension (makes sense, since NO dilates). - A loud P2 and tricuspid regurgitation are HY findings in cor pulmonale. I discuss these in more detail in the tables below.
--	--

Hyper-quick causes of bilateral pitting peripheral edema	
Cardiac	<ul style="list-style-type: none"> - Right heart failure (either due to cor pulmonale or congestive) → ↓ ability to fill right heart → ↑ central venous pressure → ↑ systemic venous hydrostatic pressure → transudation of fluid from systemic veins/venules into interstitium of legs. - Answer on NBME for why HTN doesn't automatically cause peripheral edema → answer = "increased pre-capillary resistance." In other words, arterioles are responsible for the majority of peripheral resistance; in the setting of high BP, the reason capillary hydrostatic pressure isn't automatically high enough where the transudation threshold is reached is because arterioles constrict, thereby ↑↑ resistance and reducing excessive blood flow through the capillaries.
Hepatic	<ul style="list-style-type: none"> - Cirrhosis → ↓ hepatic production of albumin → ↓ intravascular oncotic pressure → transudation of fluid from systemic veins/venules into interstitium of legs.
Nephrogenic	<ul style="list-style-type: none"> - Proteinuria → hypoalbuminemia → ↓ intravascular oncotic pressure → transudation of fluid from systemic veins/venules into interstitium of legs.
Drugs	<ul style="list-style-type: none"> - Dihydropyridine calcium channel blockers (i.e., amlodipine, nifedipine). - Imatinib (targets BCR/ABL tyrosine kinase in CML). - Miscellaneous mechanisms not important for USMLE. Just know above drugs do it.
Dietary	<ul style="list-style-type: none"> - Strict vegetarianism or veganism → ↓ dietary protein consumption → ↓ intravascular oncotic pressure → transudation of fluid from systemic veins/venules into interstitium of legs.
Pregnancy	<ul style="list-style-type: none"> - A little bit of peripheral edema is normal in pregnancy due to compression of IVC.

Hyper-quick causes of unilateral non-pitting edema	
Lymphatic insufficiency	<ul style="list-style-type: none"> - Malignancy (e.g., peau d'orange of breast), Hx of surgery (e.g., mastectomy), <i>Wuchereria bancrofti</i> (elephantiasis).
Thyroid	<ul style="list-style-type: none"> - Pretibial myxedema (Graves) → mucopolysaccharide deposition in skin + surrounding edema. - Myxedema (severe hypothyroidism) → despite the name, it refers to general "severe hypothyroidism," not just skin changes; can cause carpal tunnel syndrome. - "Pretibial myxedema" is only seen in Graves. Paradoxical hyperthyroidism seen in Hashimoto causing pretibial myxedema is astronomically rare and will get you questions wrong on USMLE.

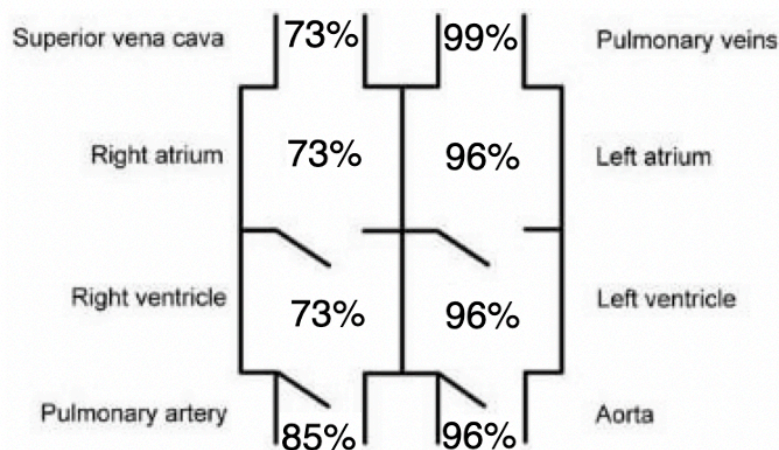
HY Valvular / flow abnormalities on USMLE	
Atrial septal defect	<ul style="list-style-type: none"> - Fixed splitting of S2. - Can sometimes be associated with a systolic flow murmur, since more blood L → R from the LA → RA means more blood flow across the pulmonic valve. So Q might say "fixed splitting of S2 and a systolic murmur." - Sometimes can be seen in Qs as "wide, fixed splitting." I only mention this because some students get pedantic / ask about this. "Wide splitting"

	<p>just means right ventricular hypertrophy. So if the Q says “wide, fixed splitting,” they’re saying the patient has RVH due to an ASD.</p> <ul style="list-style-type: none"> - Patent foramen ovale = ASD on USMLE. Don’t confuse with patent ductus arteriosus (discussed below). - USMLE loves asking questions (on 2CK, yes) showing you change in oxygen in the chambers of the heart and making you choose ASD, VSD, etc.  <ul style="list-style-type: none"> - For example, you can see above that somehow O₂ increases from the SVC to the RA, which is ordinarily impossible. The only way this could occur is if an ASD is present, where oxygenated blood moved from LA → RA. - ASDs can sometimes be responsible for “paradoxical emboli,” where a DVT leads to stroke. This is ordinarily impossible, since a clot embolizing to the lungs via the venous circulation has no way of reaching the arterial circulation. But if an ASD is present, the clot can go RA → LA → LV → up to the brain, causing stroke. - ASDs do not need to be repaired unless patient has evidence of pulmonary hypertension, RVH, arrhythmia (usually AF), or paradoxical embolus.
Ventricular septal defect	<ul style="list-style-type: none"> - Holosystolic (aka pan-systolic) murmur at lower left sternal border. - Can be associated with a diastolic rumble or enlarged left atrium (if more blood going L → R across VSD, then more blood is returning to the LA from the lungs → LA dilatation). - Seen as part of tetralogy of Fallot (VSD, RVH, overriding aorta, pulmonic stenosis). - If a VSD is repaired, USMLE wants ↑ LV pressure, ↓ RV pressure, and ↓ LA pressure as the changes now seen in the heart. - VSD does <i>not</i> cause cyanosis at birth. Only years later after the higher blood flow to the lungs results in pulmonary hypertension, followed by right ventricular hypertrophy and reversal R → L (Eisenmenger) does the patient become cyanotic. - Murmur can be silent or soft at birth, followed by loud at 7 days of life. The USMLE will ask why the murmur is louder now → answer = decreased pulmonary vascular resistance – i.e., the lungs open up during the first week of life, resulting in decreased RV pressure and an increase in the L → R pressure gradient (louder murmur). - Conversely, if they ask why the murmur was softer at birth compared to now, the answer is “increased pulmonary vascular resistance,” where the lungs were still closed at the time, so there was a lesser gradient L → R (softer murmur). - Similar to ASD Qs, USMLE loves giving you diagrams with changes in O₂ between the chambers and then making you infer we have a VSD. Yes, this stuff is asked on 2CK.

	 <p>- NBME loves this style of Q. You can see O₂ somehow increased from RA to RV. The only way this is possible is if we have a VSD where oxygenated blood moves from LV → RV.</p>  <p>- This one might initially appear a little more difficult. This is Eisenmenger syndrome, where we have a reversal of flow from RV → LV across the VSD. The NBME is known to show this diagram as well.</p> <ul style="list-style-type: none"> - If you're wondering why oxygen % goes from 99 to 96 from the pulmonary circulation to the LA, this is because of thebesian veins draining the myocardium itself, which open into the different heart chambers, including the LA. If you think that's weird, take it up with NBME, not me, since they have the 99 to 96 drop-down on their diagrams. - VSDs are repaired if patient develops pulmonary hypertension, RVH, arrhythmia, Eisenmenger syndrome, recurrent endocarditis (turbulence of blood due to VSD can ↑ risk of valve infections), or aortic regurgitation (if VSD located near the aortic valve).
Atrioventricular septal defect	<ul style="list-style-type: none"> - Seen in Down syndrome. - Between the atrium and ventricle, aka "endocardial cushion defect," although this latter term can also apply to ASD and VSD in Downs.
Mitral regurgitation	<ul style="list-style-type: none"> - Holosystolic (pan-systolic) or just regular "systolic," 29 times out of 30. - Most USMLE questions will not mention it radiating to the axilla. - Highest yield cause of MR on USMLE is post-MI papillary muscle rupture. USMLE is obsessed with this. They'll say hours to days after an MI, patient has new-onset systolic murmur → answer = MR. - Seen acutely in rheumatic heart disease (valve scars over years later and becomes mitral stenosis).

	<ul style="list-style-type: none"> - Can be caused by general ischemia / dilated cardiomyopathy. - Can cause JVD (i.e., back up all the way to the right heart); this is asked multiple times on the new NBMEs. - You do not do preoperative stress tests to determine perioperative MI risk if the patient has mere mitral regurg without other risk factors. For example, one of the 2CK forms gives a Q where smoker with MR has no shortness of breath or chest pain with exertion, and the answer is “no further management indicated,” where exercise stress test is wrong. - If the patient has Sx of heart failure or ischemia, then we do pre-op stress test to determine MI risk. I discuss stress tests later in this chapter. - The mitral valve is replaced if the patient develops severe pulmonary symptoms (i.e., shortness of breath / reduced exercise tolerance), reduced ejection fraction, arrhythmia, or endocarditis if valve function is destroyed.
Mitral stenosis	<ul style="list-style-type: none"> - Described as “rumbling diastolic murmur with an opening snap”; can also be described as “decrescendo mid-late diastolic murmur” (i.e., following the opening snap). - Can cause a right-sided S4 if the pressure backs up all the way to the right heart (seen on NBMEs sometimes; this confuses students because they think S4 must be LV, but it’s not the case). An S4 is a diastolic sound heard in either the LV or RV when there is diastolic stiffening due to high afterload. - 99% of mitral stenoses are due to Hx of rheumatic heart disease (i.e., the patient had rheumatic fever as a child, where at the time it was mitral regurg, but years later it has now become mitral stenosis). - One 2CK NBME Q mentions patient with history of rheumatic heart disease who, years later, now has 4/6 rumbling diastolic murmur without an opening snap; this is still mitral stenosis. Although opening snap is buzzy for MS, just be aware it’s not mandatory and that this Q exists on NBME. - Other HY presentation on USMLE is pregnant women with new-onset dyspnea in 2nd trimester and a diastolic murmur. This is because 50% increase in plasma volume by 2nd trimester causes the underlying subclinical MS to become symptomatic. Don’t confuse this with severe dyspnea and peripheral edema in late third-trimester, which is instead peripartum cardiomyopathy (antibody-mediated). - The 1% of MS that’s not due to Hx of RF can be marantic (non-bacterial thrombotic endocarditis; NBTE) → endocarditis seen due to hypercoagulable state in the setting of malignancy, where the vegetations are small and verrucous, on both sides of the valve. This is in contrast to bacterial endocarditis, which causes large, floppy vegetations that lead to MR, not MS. - Libman-Sacks endocarditis seen in SLE is due to antiphospholipid antibodies and is a type of NBTE. - Balloon valvuloplasty is the 1st-line Tx for mitral stenosis. This is done if patient has minimal calcification of the valve + has pulmonary HTN. - Mitral valve replacement is done if balloon valvuloplasty fails, if patient has severe MS with dyspnea, arrhythmia, or calcification of the valve.
Mitral valve prolapse	<ul style="list-style-type: none"> - Most common murmur. - Described as mid-systolic click. - “Myxomatous degeneration” is buzzy term that refers to connective tissue degeneration causing MVP in Marfan and Ehlers-Danlos. - Almost always asymptomatic. On 2CK forms, they want you to know about “mitral valve prolapse syndrome,” which is symptomatic MVP that presents as repeated episodes of “fleeting chest pain” on the left side in an otherwise healthy patient 20s-30s. They might say there is Hx of MI in the family, but this is MVPS, not MI. Answer on NBME is “no Tx necessary.”

	<ul style="list-style-type: none"> - USMLE loves using MVP as a distractor in panic disorder questions. They will give long paragraph about panic attack/disorder + also mention there's a mid-systolic click; they'll ask for cause of patient's presentation → answer = panic disorder, not MVP → student is confused because they say mid-systolic click, but the MVP isn't the cause of the patient's presentation; the panic disorder is; MVP's are usually incidental, benign, and asymptomatic. - MVP does not progress to mitral regurg almost always. So don't think that MVP and MR are the same.
Aortic regurgitation	<ul style="list-style-type: none"> - Decrescendo holo-diastolic (pan-diastolic) murmur; can also be described as "early diastolic murmur," or "diastolic murmur loudest after S2." - Causes wide pulse pressure (i.e., big difference between systolic and diastolic pressures, e.g., 160/50, or 120/40) → results in head-bobbing and bounding pulses (don't confuse with slow-rising pulses of aortic stenosis). - The bounding pulses can be described on NBME as "brisk upstroke with precipitous downstroke." In turn, they can just simply say, "the pulses are brisk," meaning the systolic component is strong. - I would say 4/5 times bounding pulses means AR. The other 1/5 will be PDA and AV fistulae (discussed below). Bounding pulses occur when blood quickly leaves the arterial circulation. In AR, the blood quickly collapses out of the aorta back into the LV. In PDA, it leaves the aorta and enters the ductus arteriosus; in AV fistulae, it leaves for a vein. - Highest yield cause on USMLE is aortic dissection → can retrograde propagate toward the aortic root causing aortic root dilatation and AR. - Even though MVP is most common in Marfan and Ehlers-Danlos, AR is second most common in these patients, since if they get aortic dissection, this can lead to AR. - Can lead to volume overload on the LV and eccentric hypertrophy. - Valve is replaced if patient has EF <50%, there is significant left ventricular dilatation, or if severe endocarditis has obliterated the valve.
Aortic stenosis	<ul style="list-style-type: none"> - Mid-systolic murmur, or just "systolic" murmur; can also be described as "late-peaking systolic murmur with an ejection click." - Radiates to the carotids. This descriptor shows up quite frequently on NBME (way more than radiation to the axilla for MR). - Causes slow-rising pulses, aka "pulsus parvus et tardus" (don't confuse with bounding pulses of AR). - SAD → Syncope, Angina, Dyspnea; classic combination seen in AS, albeit not mandatory. If you get a question where they say systolic murmur but you're not sure of the diagnosis, if they say chest pain or fainting, you know it's AS. - Often caused by bicuspid aortic valve. The patient need not have Turner syndrome and often won't. Bicuspid valve is usually inherited as an autosomal dominant familial condition. - The bicuspid valve need not calcify in middle-age prior to the AS forming. Bicuspid valve can present with AS murmur in child or high schooler. - Do aortic valve replacement on 2CK if 1) cross-section of valve is <1.0 cm², or 2) there is SAD. They ask both of these as separate Qs where they want valve replacement.
Tricuspid regurgitation	<ul style="list-style-type: none"> - Will be described on USMLE as a holosystolic murmur that increases with inspiration. - Right-sided heart murmurs get worse with inspiration → diaphragm moves down → decreased intra-thoracic pressure → increased right-heart filling. - Can cause pulsatile liver. - Highest yield cause of TR on USMLE is pulmonary hypertension / cor pulmonale. I see this all over the NBME exams. For whatever reason, these




	<p>conditions do not cause pulmonic regurg; they cause tricuspid regurg. In other words, if you see tricuspid regurg in a Q, your first thought should be pulmonary hypertension or cor pulmonale (right heart failure due to a pulmonary cause).</p> <ul style="list-style-type: none">- IV drug user endocarditis is obvious risk factor for TR, but weirdly nonexistent on USMLE.- Carcinoid syndrome is theoretical cause but lower yield.																											
Tricuspid stenosis	<ul style="list-style-type: none">- Nonexistent murmur on USMLE. I don't think I've ever seen this assessed once on any NBME exam for Steps 1 and 2 combined.- In theory, would be a rumbling diastolic murmur similar to mitral stenosis, but would increase with inspiration since it's on the right side of the heart.																											
Pulmonic regurgitation	<ul style="list-style-type: none">- Same as with tricuspid stenosis, this is a nonexistent murmur on USMLE. I've never seen it assessed.- In theory it would be the same as aortic regurg but on the right (i.e., holo-diastolic murmur), but increases with inspiration.																											
Pulmonic stenosis	<ul style="list-style-type: none">- Seen in tetralogy of Fallot.- Described as mid-systolic murmur, or just regular "systolic" murmur, that increases with inspiration, at the left sternal border, 2nd intercostal space. This is the theoretical location, whereas AS is the 2nd intercostal space on the right, not left. But the USMLE often isn't strict about murmur locations this way.																											
Patent ductus arteriosus (PDA)	<ul style="list-style-type: none">- Ductus arteriosus is special vessel in fetal circulation that connects the proximal pulmonary trunk to the descending arch of the aorta. This allows for blood to bypass the high-resistance lungs <i>in utero</i>. After birth, this vessel should close, resulting in a remnant called the ligamentum arteriosum, but sometimes it does not close → PDA.- If a PDA occurs, blood moves in the neonate L→R (i.e., opposite of <i>in utero</i>) from the descending arch of the aorta to the pulmonary trunk. <div><p>The diagram illustrates the flow of blood between the right and left sides of the heart and major vessels in the context of a Patent Ductus Arteriosus (PDA). The flow percentages are as follows:</p><table><tr><th>From</th><th>To</th><th>Percentage</th></tr><tr><td>Superior vena cava</td><td>Right atrium</td><td>73%</td></tr><tr><td>Right atrium</td><td>Right ventricle</td><td>73%</td></tr><tr><td>Right ventricle</td><td>Pulmonary artery</td><td>85%</td></tr><tr><td>Pulmonary artery</td><td>Pulmonary veins</td><td>99%</td></tr><tr><td>Pulmonary veins</td><td>Left atrium</td><td>96%</td></tr><tr><td>Left atrium</td><td>Left ventricle</td><td>96%</td></tr><tr><td>Left ventricle</td><td>Aorta</td><td>96%</td></tr><tr><td>Aorta</td><td>Pulmonary artery (via PDA)</td><td>96%</td></tr></table></div> <ul style="list-style-type: none">- You can see in the above diagram, somehow the blood become more oxygenated from the RV to the pulmonary artery, which is ordinarily impossible. The only way this could have occurred is if oxygenated blood came L→R from the aorta to the pulmonary artery via a PDA.- Murmur described three ways on USMLE: 1) continuous, machinery-like murmur; 2) pan-systolic pan-diastolic murmur (meaning it's continuous throughout both systolic and diastole); and 3) to-and-fro. The latter shows up on 2CK offline NBME 6.- Classically associated with congenital rubella (HY). They'll give a kid born with a PDA and then ask what the mom experienced while pregnant; answer = arthritis and/or rash (rubella often presents as arthritis in adults)	From	To	Percentage	Superior vena cava	Right atrium	73%	Right atrium	Right ventricle	73%	Right ventricle	Pulmonary artery	85%	Pulmonary artery	Pulmonary veins	99%	Pulmonary veins	Left atrium	96%	Left atrium	Left ventricle	96%	Left ventricle	Aorta	96%	Aorta	Pulmonary artery (via PDA)	96%
From	To	Percentage																										
Superior vena cava	Right atrium	73%																										
Right atrium	Right ventricle	73%																										
Right ventricle	Pulmonary artery	85%																										
Pulmonary artery	Pulmonary veins	99%																										
Pulmonary veins	Left atrium	96%																										
Left atrium	Left ventricle	96%																										
Left ventricle	Aorta	96%																										
Aorta	Pulmonary artery (via PDA)	96%																										

	<ul style="list-style-type: none"> - Indomethacin (NSAID) will close the PDA. - Prostaglandin E1 is used to keep a PDA open (if a kid with congenital heart malformations is born cyanotic and we need to buy time until surgery). - An open PDA can mask cyanosis in a newborn in a variety of conditions (i.e., hypoplastic left heart syndrome or pre-ductal coarctation). If they tell you a kid is born with normal APGAR scores but a week later becomes cyanotic and they ask why, the answer is "closure of ductus arteriosus."
Tetralogy of Fallot	<ul style="list-style-type: none"> - 1) Pulmonic stenosis; 2) RVH; 3) overriding aorta; 4) VSD. - If you're asked which component most determines prognosis, the answer is the degree of pulmonic stenosis. - The child will not be cyanotic at birth, but then years later, will develop Eisenmenger syndrome (i.e., a reversal of the $L \rightarrow R$ shunt over the VSD to be $R \rightarrow L$) and cyanosis, where the stem gives a school-age kid who squats on the playground to relieve symptoms. - Squatting \uparrow afterload, which \uparrow LV pressure, which \downarrow the pressure gradient of the $R \rightarrow L$ shunt, thereby mitigating cyanosis. - Squatting also \uparrow preload by \uparrow venous return back to the right heart. But it is the effect of \uparrow afterload that is most related to the \downarrow in symptoms. - Tx is surgical correction in infancy or early childhood.
Functional (flow) murmur	<ul style="list-style-type: none"> - Systolic murmur seen in the setting of higher heart rate caused by infection, anemia, or pregnancy. Caused by increased flow across the pulmonic and/or aortic valves. - Known as a functional murmur because this means it goes away once the heart rate comes back down. - Seen all over 2CK forms for kids, where they try to trick you into thinking the kid has a valvular pathology of some kind, but there isn't; there will merely be an infection or simple viral infection. - Can be seen sometimes with ASD, where the patient will have fixed splitting of S2 "plus a systolic murmur" \rightarrow merely higher right-sided volume, so more flow across the pulmonic valve.
Venous hum	<ul style="list-style-type: none"> - On 2CK form; described as a murmur in the neck that abates when the kid is laid supine + the neck rotated. - Benign + don't treat.
"Ball-in-valve" murmur	<ul style="list-style-type: none"> - Associated with cardiac tumors (i.e., myxoma in adult, or rhabdomyoma in kids for tuberous sclerosis). - Described as a diastolic rumbling murmur that abates when the patient is re-positioned unconventionally (e.g., onto his or her right side).
Persistent fetal hypertension	<ul style="list-style-type: none"> - Aka persistent fetal circulation. - Q will give a post-term birth at 42 or 43 weeks + meconium-stained fluid + echo of the neonate shows a $R \rightarrow L$ shunt across the foramen ovale. Student says, "Wait, but isn't the foramen ovale between the atria, and that's only open in the fetus but is supposed to close after birth?" Correct. Hence we have <i>persistent</i> fetal circulation. - Answer on USMLE will be "failure of pulmonary vasodilation." Meconium aspiration syndrome can \downarrow opening of the lung vasculature, leading to \uparrow right heart pressure and \uparrow risk of persistent fetal circulation.
S3 versus S4	<ul style="list-style-type: none"> - Both are diastolic sounds. - S3 is due to high volume/preload in the left ventricle, causing a reverberation against the wall. - S3 can sometimes be physiologic (i.e., normal / no problem) in pregnancy and high-endurance athletes. Patient will have eccentric hypertrophy (sarcomeres laid in linear sequence). If pathologic, it is due to dilated cardiomyopathy with reduced ejection fraction ($<55\%$) or high-output cardiac failure ($EF >70\%$).


	<ul style="list-style-type: none"> - There is one question on IM CMS form 7 where they give an S3 in diastolic dysfunction. I'm convinced this is an erratum, but I need to mention it because it exists on the NBME form. - S4 is due to high pressure/afterload on the left (but sometimes right) ventricle, causing a stiffened ventricle with diastolic dysfunction and concentric hypertrophy (sarcomeres laid in parallel). It is always pathologic. It is usually caused by systemic hypertension causing afterload on the LV, or aortic stenosis. - S4 can sometimes be right-sided on USMLE. There is a 2CK Q where they give severe mitral stenosis and say there's an S4, but it's for the RV not LV. Some weird/annoying points: <ul style="list-style-type: none"> - The combo of S3 and S4, seen together in the same vignette, can be seen in high-output cardiac failure. For example, they will say a patient as an AV fistula/conduit, or has Paget disease, and they will say there's S3 and S4 and ask for diagnosis → answer = high-output cardiac failure. The take-home point is that high-output failure can present with either an isolated S3 or the combo of S3 and S4 together, but never S4 alone on USMLE.
Loud P2	<ul style="list-style-type: none"> - One of the highest yield cardiac sounds on USMLE, almost always overlooked by students. - Means pulmonary hypertension or cor pulmonale on USMLE. - The pulmonic valve slams shut due to high pressure distal to it. - For example, they'll give a smoker who simply has a loud P2 → this just means patient has pulmonary hypertension. Not complicated. - Also recall that I said above that highest yield cause of tricuspid regurg on USMLE is pulmonary hypertension / cor pulmonale. So both what I want you to remember is both TR and loud P2 for this. - Sometimes the USMLE will just say "loud pulmonic component of S2," or "loud S2," rather than saying "loud P2." I've never seen "loud A2" on USMLE, but in theory this means systemic hypertension. - A soft P2 refers to pulmonic stenosis, but is LY.
Wide splitting of S2	<ul style="list-style-type: none"> - Means right ventricular hypertrophy on USMLE. - A2 and P2 are far apart. - You don't have to worry about the mechanism. But in short, the more pressure you have in a ventricle, the more delayed the semilunar valve will close. So if we have RVH, P2 occurs later, widening the split. - Wide splitting of S2, right-axis deviation on ECG, and right bundle branch block (RBBB) all = right ventricular hypertrophy on USMLE.
Paradoxical splitting of S2	<ul style="list-style-type: none"> - Means left ventricular hypertrophy on USMLE. - A2 occurs after P2 (normally we have A2 before P2). - Left ventricular pressure is high and A2 delayed to the point that it actually occurs on the opposite side of P2. - Paradoxical splitting of S2, left-axis deviation on ECG, and left bundle branch block (LBBB) all = left ventricular hypertrophy on USMLE.
Coarctation of the aorta	<ul style="list-style-type: none"> - Refers to narrowing of the aortic arch (this is referred to as coarctation; do not use the word stenosis to describe this). - Classically seen in Turner syndrome, but absolutely not mandatory. Shows up idiopathically in plenty of NBME Qs. I point this out because students often think the patient must have Turner syndrome. - Presents as upper extremities that have higher BP, brisk pulses, and are warmer; the lower extremities have lower BP, weak pulses, and are cooler. - Sometimes the Q can just say, "the radial pulses are brisk." → The implication is, "Well if they're saying specifically that the radial pulses are brisk, that must mean the pulses in the legs aren't." - Murmur sound not important for USMLE. Can sometimes be described as a systolic murmur heart in the infrascapular region. - Can cause LVH with left-axis deviation ECG.

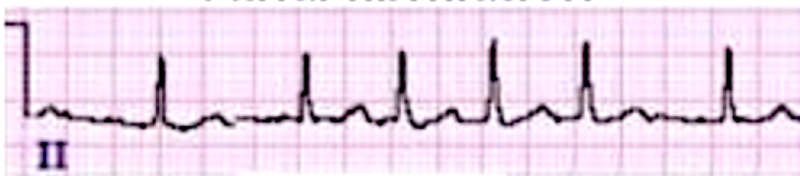
	<ul style="list-style-type: none"> - USMLE doesn't give a fuck about pre- vs post-ductal. Pre-ductal in theory will be a very sick neonate. Post-ductal will be an adult (most cases).
Subclavian steal syndrome	<ul style="list-style-type: none"> - The vertebral artery (goes to brain) is the first branch of the subclavian artery (goes to arm). - If there is a narrowing/stenosis of the proximal subclavian prior to the branch point of the vertebral artery, this can lead to lower pressure in the vertebral artery. - This can cause a backflow of blood in the vertebral artery, producing miscellaneous neuro findings such as dizziness. - Blood pressure is different between the two arms. - USMLE will ask the Q one of two ways: 1) they'll give you dizziness in someone who has BP different between the arms and then ask for merely "subclavian steal syndrome," or "backflow in a vertebral artery" as the answer. Or 2) they'll give you BP in one of the arms + give you dizziness, then the answer will be, "Check blood pressure in other arm." - Next best step in Dx is CT or MR angiography (asked on 2CK NBME). - I should point out that probably 3/4 questions on USMLE where blood pressure is different between the arms, this refers to aortic dissection. But 1/4 is subclavian steal syndrome. As per my observation.
Vertebral artery stenosis	<ul style="list-style-type: none"> - Presents same as subclavian steal syndrome with otherwise unexplained dizziness, but blood pressure is not different between the arms because the subclavian is not affected. - Caused by atherosclerosis. CT or MR angiography can diagnose. - "Vertebrobasilar insufficiency" is a broader term that refers to patients who have either subclavian steal syndrome or vertebral artery stenosis.
Vertebral artery dissection	<ul style="list-style-type: none"> - 2CK forms assess vertebral artery dissection, where they want you to know a false lumen created by dissection in a vertebral artery can lead to stasis and clot formation, which in turn can embolize to the brain and cause stroke. - NBME can mention recent visit to a chiropractor (neck manipulation is known cause). - The answer on the NBME is heparin for patients who have experienced posterior stroke due to vertebral artery dissection. Sounds weird because it's arterial, but it's what USMLE wants.
Carotid artery dissection	<ul style="list-style-type: none"> - Shows up on 2CK form as patient with stroke-like presentation + who simultaneously has ipsilateral facial/neck pain. - The pain is due to stretching of nociceptors secondary to vascular dilation. - Stasis within false lumen can lead to embolus to brain/eye.
Carotid artery stenosis	<ul style="list-style-type: none"> - Caused by atherosclerosis. - HTN biggest risk factor for atherosclerosis specifically of the carotids (strong systolic impulse pounds the carotids → endothelial damage → atheromatous plaque formation). - Carotid bruit only seen in about 25% of Qs. Don't rely on this as crutch. - Vignette will give a stroke, TIA, or retinal artery occlusion in the setting of a patient with HTN. → You have to be able to make the association that a plaque from one of the carotids has launched off, since HTN = ↑ risk. - USMLE will then ask for management (2CK only): - Do carotid duplex ultrasonography as next best step in diagnosis to look for degree of occlusion. I've never seen carotid angiography as a correct answer on NBME exams. - If occlusion >70% symptomatic, or >80% asymptomatic, then do endarterectomy. "Symptomatic" = stroke, TIA, or retinal artery occlusion. A mere bruit is not a symptom; that is a sign. - If under these thresholds, do medical management only, which requires a triad of: 1) statin; 2) ACEi or ARB; and 3) anti-platelet therapy.



	<ul style="list-style-type: none"> - The USMLE will not force you to choose between low- and high-potency statins. - USMLE tends to list lisinopril as their favorite ACEi for HTN control. - It's to my observation aspirin alone is sufficient on NBME exams for anti-platelet therapy, even though in real life patient can receive either aspirin alone; the combo of aspirin + dipyridamole; or clopidogrel alone. - USMLE will not give borderline carotid occlusion thresholds – i.e., they'll say either 30% or 90%. If they list the % as low, look at the vignette for the drugs they list the patient on. Sometimes they'll show the patient is already on statin, lisinopril, and aspirin, and then the answer is just "continue current regimen." I have once seen "add clopidogrel" as a wrong answer in this setting, which makes sense, since the combo of aspirin + clopidogrel is never given anyway. - Sometimes they will give you a low carotid occlusion % + say the patient is on 2 of 3 drugs in the triad, and then the answer is just "add aspirin," or "add statin," or "add lisinopril." - If the vignette doesn't mention elevated BP but says you have some random dude over 50 with a stroke, TIA, or retinal artery occlusion, the next best step is carotid ultrasonography to look for carotid stenosis. In other words, it is assumed the patient has a carotid plaque in this setting. - If the vignette gives patient with episodes of unexplained <i>syncope</i> or light-headedness, but not stroke, TIA, or retinal artery occlusion, then the next best step is ECG, followed by Holter monitor, looking for atrial fibrillation (AF causes LA mural thrombus that launched off to brain/eye). - The triad of 1) statin; 2) ACEi or ARB; and 3) anti-platelet therapy is also done for general peripheral vascular disease unrelated to carotid stenosis (i.e., if a patient has intermittent claudication). - Stroke, TIA, or retinal artery occlusion, if they don't mention HTN, but they mention an <i>abdominal</i> bruit, you will still do a carotid duplex ultrasound. The implication is that the bruit in the abdomen could be a AAA or RAS, where atherosclerosis in one location means atherosclerosis everywhere, so the patient likely has carotid stenosis by extension. They once again need not mention carotid bruit; apparently it is not a sensitive finding (i.e., we cannot rule-out ↑ occlusion just because we don't hear it).
Aortic dissection	<ul style="list-style-type: none"> - Classically presents as severe upper chest pain radiating to the back between the scapulae. - As discussed above in the aortic regurg section, USMLE loves this as most common cause of AR due to retrograde propagation toward the aortic root. For example, patient with Hx of HTN, cocaine use, or a connective tissue disorder (i.e., Marfan, Ehlers-Danlos) who has a diastolic murmur, you should be thinking immediately that this is dissection. - "Medial necrosis" is a term that is used on NBME exams to describe changes to the aorta in dissection. In the past, "cystic medial necrosis" used to be buzzy for dissection due to Marfan syndrome, but I haven't seen USMLE care about this. I have, however, seen a dissection Q on NBME where it is due to hypertension, and simply "medial necrosis" is the answer. - As mentioned above, 3/4 Qs where BP is different between the arms refers to aortic dissection. A Q on 2CK IM form 7 has "thoracic aortic dissection" where not only is the BP different between the arms, but it's also different between the L and R <i>legs</i> (i.e., L-leg BP is different from R-leg BP) → sometimes thoracic aortic dissections can anterograde propagate all the way down to the abdominal aorta.


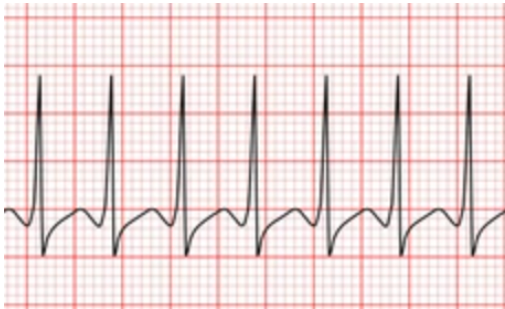
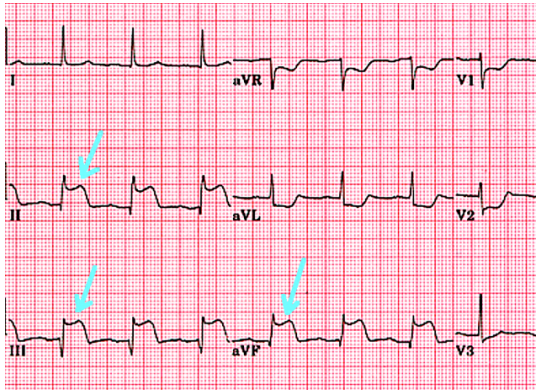
	<div> <div> <div>De Bakey Type I</div>  <div>Stanford</div> </div> <div> <div>Type II</div>  <div>Type A</div> </div> <div> <div>Type III</div>  <div>Type B</div> </div> </div> <p> - You do not need to memorize these aortic aneurysm types. I'm just showing you that if the common iliacs are involved (as with left image), BP can differ as well <i>between the legs</i>. For 2CK: - Tx for ascending aortic aneurysm (type A) = labetalol + surgery. - Tx for descending aortic aneurysm (type B) = labetalol alone initially. </p>
Traumatic rupture of the aorta	<p> - Caused by deceleration injury. Most common cause of death due to car accident or fall. Exceedingly HY on 2CK. - Will be described as patient following an MVA who has "widening of the mediastinum." They'll then ask for the next best step → answer = aortic angiography (aka aortography), OR CT angiography. - New 2CK form has "CT scan of the chest" straight up as the answer, which refers to CT angiography. NBME/USMLE will not force you to choose between aortography or CT angiography; they'll just list one. - Labetalol used first-line in patients who have aortic dissection and traumatic rupture of the aorta. Nitroprusside comes after. - Labetalol is answer on NBME even in patient who has <i>low BP</i> due to rupture or dissection due to the drug ↓ shearing forces. I've seen students get this wrong saying, "But patient has low BP though." My response is, file a complaint with the exam not with me. - 2CK Q gives "esmolol + nitroprusside" as answer to a traumatic rupture Q, but almost always, they will just want "labetalol." - Emergency surgical repair is indicated following IV drug administration. </p>
Aortic aneurysm	<p> - Can present as "visible pulsation" on USMLE. - For aortic aneurysm, they can say "visible pulsation above the manubrium," or "pulsatile mass above the manubrium." There can also be a tracheal shift. I've seen students select pneumothorax here. But for whatever reason you can get tracheal shift in thoracic aortic aneurysm. For AAA, there can be "visible pulsation in the epigastrium." - Biggest risk factor for AAA is smoking. - For Family Med, do a one-off abdominal ultrasound in men 65+ who are ever-smokers. - For Surgery, AAA repair is indicated if the aneurysm is >5.5 cm or the rate of change of size increase is >0.5cm over a 6-month period. This is on Surgery form, where they give a patient with a 4-cm AAA and ask why serial ultrasounds are indicated → answer = "size of aneurysm." - In general, perioperative MI risk is assessed using a pre-op stress test. 2CK NBME Q has dipyridamole and thallium pharmacologic stress test as answer in patient with 6-cm AAA prior to surgery. </p>

	<ul style="list-style-type: none"> - Diabetes is protective against aneurysm. Non-enzymatic glycosylation of endothelium causes stiffening of the vascular wall. - Don't do AAA repair on USMLE in patient who has advanced comorbidities or terminal disease, e.g., stage 4 lung cancer. - Tangential: 2CK loves "pulsatile hematoma" in the neck in trauma patients, where the answer is "endotracheal intubation." Sounds nitpicky, but shows up repeatedly.
Arteriovenous fistula	<ul style="list-style-type: none"> - Can be idiopathic, iatrogenic (i.e., dialysis), from injury (i.e., stab wound), or caused by other disease (i.e., hereditary hemorrhagic telangiectasia or Paget disease of bone). - Similar to aortic aneurysms, AV fistulae can sometimes present with pulsatile mass, <i>but in a weird location</i>, e.g., around the left ear in patient with tinnitus (on NBME exam). Student says, "Why is it at the left ear though?" → No fucking idea. Take it up with NBME. - Highest yield point is they can cause high-output cardiac failure. This is because blood quickly enters the venous circulation from the arterial circulation → combo of ↑ preload back to right heart + poorer arterial perfusion distal to the fistula → compensatory ↑ CO. - AV fistulae can sometimes present with a continuous machinery murmur similar to a PDA, since blood is continuously flowing through it. They might say a continuous machinery-like murmur is auscultated in the leg at site of prior stab wound. - As discussed earlier, they can present with bounding pulses similar to AR. - Student says, "Well how am I supposed to know if it's AV fistula then if it sounds like other conditions too?" → by paying attention to HY points like, "Is there lone S3 or S3/4 combo or EF >70%? Is there Hx of penetrating trauma? Or does the patient have Paget? Etc." - 2CK NBME Q shows you obscure angiogram of a fistula in the leg + tells you there's a continuous machinery murmur; they ask what most likely determines prognosis in this patient → answer = "size of lesion." <div data-bbox="635 1198 1310 1805" data-label="Image"> </div> <ul style="list-style-type: none"> - NBME exam shows obscure image similar to above (without the arrow) + they tell you there's continuous murmur → answer = "size of lesion." - Another NBME Q gives 45-year-old male will nosebleeds since adolescence + S3 heart sound + dyspnea + they show you pic of tongue; they ask for the cause of dyspnea.

	 <p>- Answer = "Pulmonary arteriovenous fistula" (leading to high-output failure); diagnosis is hereditary hemorrhagic telangiectasia. USMLE will basically always show you a pic of red dots on the tongue/mouth or finger in a patient with nosebleeds.</p> <p>- Likewise, be aware intraosseous AV fistulae can occur in Paget, as mentioned before.</p>
--	---



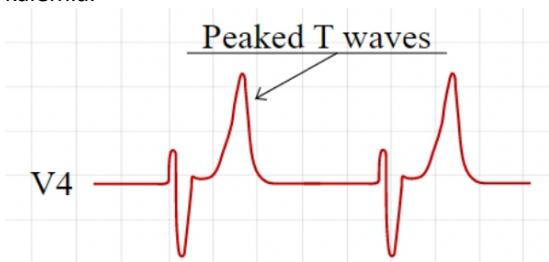
HY Murmur / ECG points for USMLE	
Atrial fibrillation (AF)	<p>- Described as "irregularly irregular" rhythm with absent p-waves.</p> <p style="text-align: center;">Atrial fibrillation</p>  <p>- Notice how the QRS complexes are at random and irregular distances from one another. This is the "irregularly irregular" pattern.</p> <p>- AF is hugely important because it can cause turbulence/stasis within the left atrium that leads to a LA mural thrombus formation. This thrombus can launch off (i.e., become an embolus) and go to brain (stroke, TIA, retinal artery occlusion), SMA/IMA (acute mesenteric ischemia), and legs (acute limb ischemia).</p> <p>- AF HY in older patients, especially over 75. Vignette will usually be an older patient with a stroke, TIA, or retinal artery occlusion, who has <i>normal</i> blood pressure (this implies carotid stenosis is not the etiology for the embolus).</p> <p>- AF usually is paroxysmal, which means it comes and goes. The vignette might say the patient is 75 + had a TIA + BP normal + ECG shows sinus rhythm with no abnormalities → next best step is Holter monitor (24-hour ambulatory ECG monitor) to pick up the paroxysmal AF (e.g., when the patient goes home and has dinner).</p> <p>- After AF is diagnosed with regular ECG or Holter, 2CK wants echocardiography as the next best step to visualize the LA mural thrombus.</p> <p>- Patient who has severe abdominal pain in setting of AF or hyperthyroidism (which can cause AF), diagnosis is acute mesenteric ischemia; next best step is mesenteric angiography; Tx is laparotomy if unstable (answer on NBME).</p>


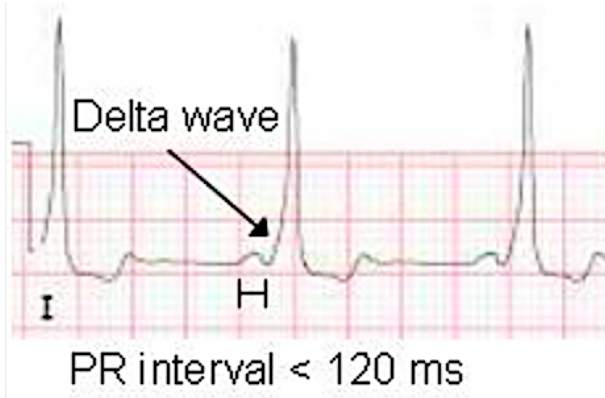
	<ul style="list-style-type: none"> - Severe pain in a leg + absent pulses in patient with irregularly irregular rhythm = acute limb ischemia; USMLE wants “embolectomy” as answer. - Any structural abnormality of the heart, either due to LV hypertrophy, ischemia, growth hormone/anabolic steroid use, prior MI, etc., can lead to AF. - You need to know AF patient will get either aspirin or warfarin. This is determined by the CHADS2 score. There are variations of the score, but the simple CHADS2 suffices for USMLE → CHF, HTN, Age 75+, Diabetes, Stroke/TIA/emboli. Each component is 1 point, but stroke/TIA/emboli is 2 points. If a patient has 0 or 1 points, give aspirin; if 2+ points, give warfarin. - “Emboli” refers to Hx of AF leading to stroke, TIA, acute, mesenteric ischemia, or acute limb ischemia – i.e., any Hx of embolic event. 2CK IM form gives short vignette of 67F with chronic AF + Hx of acute limb ischemia + no other info relating to CHADS, and answer is warfarin to prevent recurrence; aspirin is wrong. - Some students will ask about NOACs, e.g., apixaban, etc., for non-valvular AF → I’ve never seen NBME care about this stuff. They seem to be pretty old-school and just have warfarin as the answer, probably because there isn’t debate around whether it can be used; use of NOACs is less textbook. - AF patient should also be on rate control before rhythm control. The USMLE actually doesn’t give a fuck about this component of management, although in theory metoprolol or verapamil is standard. You could be aware for Step 3 that flecainide is first-line for rhythm control if patients fail rate-control and have a structurally normal heart and no coronary artery disease. - NBME for 2CK has “electrical cardioversion” as the answer for patient with AF who has hemodynamic instability (i.e., low BP). What you need to know is: sometimes AF can trigger “rapid ventricular response,” where HR goes >150 and low BP can occur.
Atrial flutter	<ul style="list-style-type: none"> - Has classic sawtooth appearance. <p style="text-align: center;">Atrial flutter</p>  <ul style="list-style-type: none"> - Low yield for USMLE. I think it’s asked once on a 2CK NBME. But as student you should know it exists / the basic ECG above.
Ventricular tachycardia (VT)	<ul style="list-style-type: none"> - Causes wide-complex QRS complexes (>120 ms; normal is 80-120 ms).  <ul style="list-style-type: none"> - Exceedingly HY for 2CK that you know VT is wide-complex, whereas SVT is narrow-complex. If you look at above ECG, even if you say, “No idea what I’m looking at.” You can tell the complexes look wide like mountains in comparison to a typical ECG.


	<ul style="list-style-type: none"> - VT is treated with anti-arrhythmics – i.e., amiodarone. If patient has coma or hemodynamic instability (low BP), the NBME answer is direct current countershock or cardioversion (same thing). - Premature ventricular complex (PVC) is asked on 2CK.  <ul style="list-style-type: none"> - Note on the above strip, we have a wide complex (meaning ventricular in origin) that occurs earlier (hence premature). What they do on the NBME is show you this strip and ask where this abnormality originates from, then the answer is just “ventricle.” - Don’t treat PVCs on USMLE.
Supraventricular tachycardia (SVT)	<ul style="list-style-type: none"> - Causes narrow / needle-shaped complexes. Make sure you’re able to contrast this with VT above, which is wide-complex.  <ul style="list-style-type: none"> - Notice the complexes are narrow / look like needles. This means the tachy originates above the ventricles (hence SVT). - Treatment of SVT exceedingly HY on 2CK. - First step is carotid massage (aka vagal maneuvers). In pediatrics, they can do icepack to the face. - If the above doesn’t work, the next step is give adenosine (not amiodarone). - Same as with VT, if the patient has coma or low BP, shocking the patient is the first step. In other words, for both SVT and VT, you must shock first in the setting of coma or hemodynamic instability. It’s for stable SVT and VT that the treatments differ on USMLE.
Acute MI (STEMI)	<ul style="list-style-type: none"> - Will present as ST-elevations in 3-4 contiguous leads. 



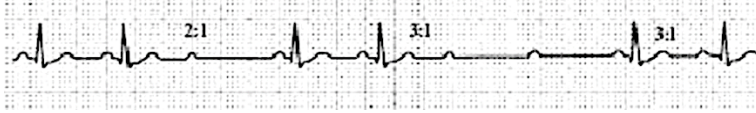

	<ul style="list-style-type: none"> - The above is an inferior MI, as evidenced by ST-elevations in leads II, III, and aVF. The answer for the affected vessel is the posterior descending artery (PDA supplies the diaphragmatic surface of the heart); since >85% of people have right-dominant circulation (meaning the PDA comes of the right main coronary), sometimes the answer for inferior MI can just be "right coronary artery." - If the Q says left-dominant circulation, the sequence USMLE wants is: left main coronary → left circumflex → PDA. - The apex of the heart is supplied by the left anterior descending artery (LAD). If there are ST-elevations in leads V1-V3, choose LAD as the answer. - The left-lateral heart is supplied by the left circumflex artery. If there are ST-elevations in leads V4-V6 for lateral MI, choose left circumflex. - Reciprocal ST-depressions in the anterior leads V1-V3 can reflex posterior wall MI (i.e., we have "elevations" out the back of the heart, so they look like depressions on the anterior wall leads). - As discussed earlier, if patient has MI followed by new-onset systolic murmur hours to days later, with or without dyspnea, that's mitral regurg. - Stroke-like presentation in patient who had MI weeks ago → "embolus from ventricular septal aneurysm" (on 2CK form). - Most common cause of death due to MI is ventricular fibrillation (VF). - Fibrosis of myocardium in the months-years post-MI increases risk of arrhythmias such as AF, SVT, VT, etc. There's no specific arrhythmia you need to memorize. Just know the risk is there in the future. - Q waves on an ECG mean old MI / history of MI. The vignette might give you patient who has light-headedness / fainting + they say patient has Q waves in II, III, aVF, and the answer will be something like "paroxysmal supraventricular tachycardia." Student thinks this specific arrhythmia matters, but it doesn't. The point is that Hx of MI means patient is at risk for nearly any arrhythmia now. - MI classically causes coagulative necrosis of the myocardium. - With cardiogenic shock as a result of MI, the arrows USMLE wants are: ↓ cardiac output, ↑ peripheral vascular resistance, ↑ PCWP. - MI can lead to acute tubular necrosis from cardiogenic shock → acute drop in renal perfusion. This is not pre-renal. I discuss this in detail in the renal section. - First treatment for MI is aspirin. After aspirin is given, the next drug to give is clopidogrel (an ADP P2Y12 blocker) as dual anti-platelet therapy. - USMLE wants you to know anyone with acute coronary syndrome (i.e., MI or unstable angina) gets coronary catheterization. This is answer on new 2CK NBME exam. - It's to my observation that more extensive management of MI on USMLE, such as use of beta-blockers, nitrates, morphine, oxygen, statin, percutaneous coronary intervention, etc., isn't assessed in detail. I can comment, however, that one 2CK Q wants you to know nitrates are contraindicated in right-heart MIs, which includes inferior MI in most people due to the right coronary supplying the PDA. This is because right-sided MIs are preload-dependent, which means they need sufficient preload to maintain BP. - Percutaneous coronary intervention (PCI) is done in patients with STEMIs within 90 minutes of reaching hospital.
Pericarditis	<ul style="list-style-type: none"> - Shows up on ECG as diffuse ST-elevations (i.e., in all leads rather than 3-4 contiguous leads as with MI). PR depressions can also be seen, but I've never seen the USMLE give a fuck about the latter. - Patient will have pain that's worse when lying back, better when leaning forward. In turn, the patient can present walking through the door bent over at the waist. - Serous pericarditis will be post-viral, secondary to autoimmune disease, or due to cocaine use. - NBME Q gives pericarditis + a bunch of different organism types (i.e., bacterium, fungus, etc.), and answer is "virus."


	<ul style="list-style-type: none"> - Patient with rheumatoid arthritis or SLE notably at risk for pericarditis. In other words, don't get confused if they mention pericardial friction rub in vignette of RA or SLE; this is common. - For cocaine use, they'll say a 22-year-old male has chest pain after a night of heavy partying + ECG shows diffuse ST-elevations → Dx = pericarditis. - Uremic pericarditis is HY for 2CK. Q will give ultra-high creatinine and BUN and say there's a friction rub → treatment = hemodialysis. - Treatment for pericarditis is same as acute gout → NSAIDs, colchicine, steroids. - Fibrinous pericarditis is post-MI and occurs as two types: 1) literally "post-MI fibrinous pericarditis," which will simply be friction rub within days of an MI; 2) Dressler syndrome (antibody-mediated fibrinous pericarditis occurring 2-6 weeks post-MI). - ECG is first step in Dx of pericarditis, but USMLE wants echocardiography as next best step in order to visualize a concomitant effusion that can occur sometimes. Vignette will give you stereotypical pericarditis + will ask for next best step in diagnosis; ECG might not be listed and you're like huh? → Answer is echocardiography to look for potential effusion concomitant to the pericarditis.
Chronic constrictive pericarditis	<ul style="list-style-type: none"> - I should make note that chronic constrictive pericarditis is a separate condition that doesn't present with the standard pericarditis findings as described above. - This is low-yield for USMLE, but students ask about it because it can be confused with tamponade. - There's two ways this can show up: <ol style="list-style-type: none"> 1) Tuberculosis is a classic cause; there may or may not be calcification around the heart on imaging. So if you get a Q where patient has TB + some sort of heart-filling impairment → answer = chronic constrictive pericarditis. 2) Kussmaul sign will be seen in the Q, where JVD occurs with <i>inspiration</i> rather than expiration. - Normally, inspiration facilitates RA filling (↓ intrathoracic pressure → ↑ pulmonary vascular compliance/stretching → ↑ high-low pressure gradient from right heart to the lungs → ↓ in afterload on RV from the lungs → blood moves easier from right heart to the lungs → blood is pulled easier from SVC/IVC to the RA). - However, if there is ↑ compressive force on the heart, the ↑ in negative intrathoracic pressure during inspiration is not transmitted to the right side of the heart, so JVP does not ↓ (and can even paradoxically can ↑). - In tamponade, however, as discussed below, the ↑ in negative intrathoracic pressure during inspiration is <i>able</i> to be transmitted to the right side of the heart, so Kussmaul sign does not occur. This is likely because in constrictive pericarditis, the rigid pericardium prevents expansion of the right heart altogether, whereas in tamponade, the pericardium isn't rigid per se, but is just filled with blood that can move/shift during the respiratory cycle, thereby allowing right heart expansion during inspiration.
Pericardial effusion / Cardiac tamponade	<ul style="list-style-type: none"> - Cardiac tamponade = pericardial effusion + low blood pressure. - What determines whether we have a tamponade or not is the <i>rate</i> of accumulation of the fluid, not the volume of the fluid – i.e., a stab wound or post-MI LV free-wall rupture resulting in fast blood accumulation, even if smaller volume, might cause tamponade, but cancer resulting in slow, but large, accumulation might not cause tamponade. - Tamponade presents as Beck triad: 1) hypotension, 2) JVD, 3) muffled/distant heart sounds. The question will basically always give hypotension and JVD. Occasionally they might not mention the heart sounds. But you need to memorize Beck triad as HY for tamponade. - Pulsus paradoxus (i.e., drop in systolic BP >10 mm Hg with inspiration) is classically associated with tamponade, although not frequently mentioned in

	<p>vignettes. I've seen a 2CK NBME Q where they say "the pulsus paradoxus is <10 mm Hg," which is their way of saying the Dx is not tamponade. I consider that wording odd, but it's what the vignette says.</p> <ul style="list-style-type: none"> - ECG will show electrical alternans / low-voltage QRS complexes.  <p>- You can see the amplitudes (i.e., heights) of the complexes are short. This refers to "low-voltage." You can also see the heights ever so slightly oscillate up and down. This refers to electrical alternans. They show this ECG twice on 2CK NBMEs.</p> <ul style="list-style-type: none"> - If the Q asks for next best step in <i>diagnosis</i>, choose ECG as first step if listed. If not listed, then choose echocardiography, which confirms fluid over the heart. - If the Q asks for next best step in management for tamponade when the vignette is obvious, choose pericardiocentesis or pericardial window. USMLE will not list both; it will be one or the other. NBME 8 offline for 2CK has pericardial window as answer, where pericardiocentesis isn't listed.
Torsades de pointes (TdP)	<ul style="list-style-type: none"> - HY type of VT that has sinusoidal pattern on ECG.  <ul style="list-style-type: none"> - USMLE wants you to know this can be caused by some anti-arrhythmic agents, such as the sodium- and potassium-channel blockers, such as quinidine and ibutilide, respectively. They ask this directly on the NBME exam, where Q will say patient is given ibutilide + what is he now at increased risk of → answer = torsades. - QT prolongation is risk factor for development of TdP. Agents such as anti-psychotics, macrolides, and metoclopramide prolong the QT. - Tx USMLE wants is magnesium (asked directly on new 2CK form), which stabilizes the myocardium in TdP.
Peaked T wave	<ul style="list-style-type: none"> - Seen in hyperkalemia.  <p>- Asked once on one of the 2CK forms, where they show the ECG.</p>

	<ul style="list-style-type: none"> - Highest yield point is that if a patient has hyperkalemia and ECG changes, the Tx USMLE wants is IV calcium gluconate or calcium chloride, which stabilizes the myocardium. Calcium gluconate is classic, but calcium chloride shows up as an answer on a 2CK NBME.
U-wave	<ul style="list-style-type: none"> - Means hypokalemia.  <ul style="list-style-type: none"> - Shows up on NBME 12 for 2CK in anorexia patient. First time I've ever seen it show up anywhere on NBME material. But Q doesn't ride on you knowing it means hypokalemia to get it right. It's HY and pass-level to know that purging (anorexia or bulimia) causes hypokalemia anyway.
Delta wave	<ul style="list-style-type: none"> - Seen in Wolff-Parkinson-White syndrome (WPW; accessory conduction pathway in heart that bypasses the AV node, resulting in reentrant SVT). - Classically described as a "slurred upstroke" of the QRS, where the PR interval is shortened.  <ul style="list-style-type: none"> - Both the delta-wave and WPW have basically nonexistent yieldness on USMLE, but I mention them here so you are minimally aware.
J waves	<ul style="list-style-type: none"> - They mean hypothermia. You don't need to be able to identify on ECG. Just know they exist, as they show up in a 2CK vignette where patient has body temperature of 89.6 F (not 98.6).

HY Heart block points for USMLE	
First degree	<ul style="list-style-type: none"> - Prolonged PR interval (>200 ms). Should normally be 80-120 ms.  <ul style="list-style-type: none"> - Note that above on the ECG, the PR-segment in particular (just prior to the QRS complex) is extra-long. - Not really assessed on USMLE. Just know the definition. - Don't treat on USMLE.

<p>Second degree Mobitz type I (aka Wenckebach)</p>	<ul style="list-style-type: none"> - Gradually prolonging PR interval until QRS drops. Then cycle repeats.  <ul style="list-style-type: none"> - Don't treat on USMLE.
<p>Second degree Mobitz type II</p>	<ul style="list-style-type: none"> - No gradual prolongation of PR interval, followed by a random dropping of the QRS.  <ul style="list-style-type: none"> - Can also sometimes occur as patterns of 2:1, 3:1, etc., where there will be a P to QRS ratio of 2:1 or 3:1, etc.  <ul style="list-style-type: none"> - Regardless as to whether the dropped QRS is random or in a numerical pattern, there is no gradual prolongation of the QRS before the dropped complex. - More dangerous than Mobitz I. This is because Mobitz II has higher chance of progression into type III heart block. - Treatment on USMLE is insertion of pacemaker. This is asked on a new 2CK NBME exam.
<p>Third degree</p>	<ul style="list-style-type: none"> - Two things you want to look for on ECG: - 1) Ultra-slow HR (i.e., 30-40). You'll see the QRS's are super far apart. This is the ventricular escape rhythm. - 2) No relationship between the P-waves and QRS complexes.  <ul style="list-style-type: none"> - Treatment on USMLE is insertion of pacemaker. - So what you want to remember is that Mobitz II and 3rd-degree are the ones where we insert pacemaker; 1st-degree and Mobitz I we don't.

HY Cardiomyopathy points for USMLE	
Dilated (DCM)	<ul style="list-style-type: none"> - Can be isolated ventricular or diffuse 4-chamber dilation. Causes are multifarious, but a key feature is systolic dysfunction, where ejection fraction is reduced (i.e., <55%, where normal range is 55-70). - CXR shows enlarged cardiac silhouette.  <ul style="list-style-type: none"> - An S3 heart sound can sometimes be heard. - Cardiac exam shows lateralized apex beat. Can be described as the point of maximal impulse being in the anterior axillary line. Should be noted that this lateralization just means an enlarged LV, so it is non-specific, and can also be seen in LV hypertrophy from any cause. But many vignettes will mention it. - The arrows USMLE wants are: ↓ EF; ↑ LVEDV; ↑ LVEDP. I discuss this stuff in more detail in my HY Arrows PDF. - Causes of DCM are ABCD: - A: Alcohol. - B: Wet Beriberi (thiamine deficiency). - C: Coxsackie B virus, Cocaine, Chagas disease. - D: Drugs → doxorubicin (aka Adriamycin). - Other notable causes are: - Pregnancy (peripartum cardiomyopathy); hemochromatosis; rheumatic heart disease (myocarditis leading to DCM).
Hypertrophic (HCM)	<ul style="list-style-type: none"> - Heart failure due to systemic hypertension. - Characterized by diastolic dysfunction (the heart can pump just fine but cannot expand as easily). - Can be associated with S4 heart sound. - The arrows USMLE wants are: ↔ EF; ↔ LVEDV; ↑ LVEDP. - Ejection fraction is normal because the heart can pump perfectly fine. - Students get confused about LVEDV, thinking it should be low, if the heart cannot expand as easily. But this is not the case for USMLE. They want you to know normal volume can be achieved; <i>it just merely requires more force/pressure to get there.</i> - As with DCM, the apex beat / point of maximal impulse can be lateralized, which merely reflects LV hypertrophy. - As described earlier, paradoxical splitting of S2, left-axis deviation on ECG, and LBBB can all be seen due to LVH. When you see these findings in vignettes, don't get confused. They just mean LVH. - Often associated with hypertensive retinopathy (fundoscopy shows narrowing of retinal vessels, flame hemorrhages, and "AV-nicking"), hypertensive nephropathy (hyperplastic arteriosclerosis with increased creatinine).

Hypertrophic obstructive (HOCM)	<ul style="list-style-type: none"> - Caused by mutations in β-myosin heavy-chain gene; autosomal dominant; results in disordered/disarrayed myocardial fibers. - HOCM causes asymmetric septal hypertrophy that results in the anterior <i>mitral</i> valve leaflet obstructing the LV outflow tract (so it can sound similar to aortic stenosis). - Classically sudden death in young athlete; cause of death is ventricular fibrillation due to acute left heart strain in the setting of fast heart rate. - Presents with systolic murmur that worsens with Valsalva or standing (aortic stenosis, in contrast, gets softer or experiences no change with Valsalva) or standing. - HOCM and MVP are the only two murmurs that get worse with less volume in the heart. All other murmurs get worse with more volume. Valsalva increases intra-thoracic pressure and decreases venous return, so there's less volume in the heart. Standing simply decreases venous return. - NBME wants you to know that \uparrow HR from exercise or stress means "diastole is shortened more than systole." - Beta-blockers (metoprolol or propranolol are both answers on NBME) are given to slow heart rate, which maximizes diastolic filling and decreasing symptoms / risk of death. - Implantable cardioverter-defibrillator (ICD) is indicated if patient develops any type of arrhythmia, syncope, low blood pressure, or LV wall thickness $>30\text{mm}$. - Septal myectomy is done if the left ventricular outflow tract pressure gradient is $>50\text{mm Hg}$. But it should be noted ICD is usually first-line.
Restrictive (RCM)	<ul style="list-style-type: none"> - Heart failure due to diastolic dysfunction, where HTN is not the cause. - JVD is HY for RCM. An S4 can also be seen. The heart will not be dilated. - HY causes are Hx of radiation (leads to fibrosis), amyloidosis, and hemochromatosis. - Student might say, "I thought you said hemochromatosis was DCM. So if we have to choose on the exam, which one is it?" The answer is, whichever the vignette gives you. If they say a large cardiac silhouette with an S3 and lateralized apex beat, that's DCM. If they say JVD + S4 + nothing about a lateralized apex beat, you know it's RCM. - Amyloidosis is protein depositing where it shouldn't be depositing. Highest yield cause of amyloidosis on USMLE is multiple myeloma, which will lead to RCM. - Since RCM is diastolic dysfunction, the arrows are the same as HCM, which are: \leftrightarrow EF; \leftrightarrow LVEDV; \uparrow LVEDP.

Atherosclerosis basic points for IM

- Most acceleratory risk factors are diabetes mellitus (I and II), followed by smoking, followed by HTN, in that order.
- HTN is most common risk factor, but DM and smoking are worse. I talk a lot about this stuff in my HY Risk Factors PDF if you want extensive detail.
- HTN is most acceleratory specifically for carotid stenosis (systolic impulse pounds carotids \rightarrow endothelial damage).
- Stroke, TIA, or retinal artery occlusion in patient with high BP is due to carotid plaque launching off to the brain/eye. If patient has normal BP, think AF instead, with left atrial mural thrombus launching off.
- Patient over 50 with Hx of cardiovascular risk factors who now has accelerated HTN, think renal artery stenosis (narrowing due to atherosclerosis).
- Plaques can calcify. The more calcium there is in a plaque, the more mature it is often considered to be. Calcium scoring is routinely done in patients who have coronary artery disease in the assessment of plaque progression.

- Statins have 2 HY MOAs on USMLE: 1) inhibit HMG-CoA reductase; 2) upregulate LDL receptors on hepatocytes.
- Ezetimibe blocks cholesterol absorption in the small bowel.
- Bile acid sequestrants (e.g., cholestyramine) result in the liver pulling more cholesterol out of the blood.
- Fibrates upregulate PPAR- α and lipoprotein lipase; best drugs to decrease triglycerides.

HY Angina points for IM	
Stable angina	<ul style="list-style-type: none"> - Chest pain that occurs predictably with exercise. - Due to atherosclerotic plaques causing >70% occlusion; can be calcific. - Classically causes ST depressions on ECG. - Nitrates (e.g., sublingual isosorbide dinitrate) used as Tx \rightarrow nitrates "donate" nitric oxide (NO) that upregulates guanylyl cyclase within venous smooth muscle \rightarrow increased cGMP \rightarrow relaxation of venous smooth muscle \rightarrow increased venous pooling of blood \rightarrow decreased venous return \rightarrow decreased myocardial oxygen demand \rightarrow mitigation of chest pain. - Nitrates are contraindicated with PDE-5 inhibitors (e.g., Viagra) due to risk of low blood pressure. - Sodium nitroprusside used for hypertensive emergencies dilates arterioles in addition to the veins. If USMLE asks you where this drug acts, choose arterioles.
Unstable angina	<ul style="list-style-type: none"> - Chest pain that is unpredictable and can occur at rest. - Due to partial rupture of atherosclerotic plaque leading to partial occlusion. - ST depressions on ECG. - Diltiazem is answer on new 2CK NBME for patient with unstable angina. - Patients need cardiac catheterization.
Prinzmetal angina (variant angina pectoris)	<ul style="list-style-type: none"> - Vasospastic angina that occurs at rest (i.e., watching TV or while sleeping) in younger adults; it is not caused by atherosclerosis. - ST elevations are seen on ECG. - You must know that Prinzmetal is also known as variant angina pectoris. There is an NBME Q that gives vignette of Prinzmetal, but answer is "variant angina pectoris." - Treatment is nitrates (can cause coronary artery dilation unrelated to the venous pooling effects) or dihydropyridine calcium channel blockers (e.g., nifedipine). Avoid α_1-agonists in these patients (cause vasoconstriction), as well as non-selective β-blockers like propranolol (can cause unopposed α effects).

Hypertensive Emergency + urgency	
Emergency	<ul style="list-style-type: none"> - HTN >180/120 + signs of end-organ damage. - The latter can be hypertensive encephalopathy (confusion), nephropathy (poor renal function tests), retinopathy, acute heart failure, etc. - BP should be \downarrow by no more than 20-25% in the first hour, as drastic \downarrow can compromise perfusion to the brain and vital organs. - Blood pressure should be brought under 160/100 by 24-48 hours. - Drugs used are IV sodium nitroprusside, IV nicardipine, IV labetalol, and oral captopril.
Urgency	<ul style="list-style-type: none"> - HTN >180/120 + no signs of end-organ damage. - Blood pressure should be brought under 160/100 by 24-48 hours. - Drugs used are IV sodium nitroprusside, IV nicardipine, IV labetalol, and oral captopril.

Shock types			
	Cardiac output (CO)	Systemic vascular resistance (SVR)	Pulmonary capillary wedge pressure (PCWP)
Cardiogenic	↓	↑	↑
Hypovolemic	↓	↑	↓
Septic	↑ (early) / ↓ (late)	↓	↓
Anaphylactic	↑ (early) / ↓ (late)	↓	↓
Neurogenic	↓	↓	↓
Obstructive	↓	↑	↓

- Septic, anaphylactic, and neurogenic are all under the envelope of distributive shock.
 - ↑ PCWP for cardiogenic is one of the highest yield path points on USMLE.
 - For deeper explanations, go to my HY Arrows PDF.


HY Endocarditis points	
Acute endocarditis	<ul style="list-style-type: none"> - Bacterial infection of valve in patient with no previous heart valve problem. - Caused by <i>Staph aureus</i> on USMLE. - Left-sided valves (i.e., aortic and mitral) most commonly affected because of greater pressure changes (i.e., from high to low) within left heart, resulting in turbulence that enables seeding. - IV drug users → venous blood inoculated with <i>S. aureus</i> → travels to heart and causes vegetation of tricuspid valve. - <i>Staph aureus</i> is coagulase positive.
Subacute endocarditis	<ul style="list-style-type: none"> - Bacterial infection of valve in patient <i>with history</i> of valve abnormality (i.e., congenital bicuspid aortic valve, Hx of rheumatic heart disease). - Caused by <i>Strep viridans</i> on USMLE. You need to know <i>S. viridans</i> can be further broken down into: <i>S. sanguinis</i>, <i>S. mutans</i>, and <i>S. mitis</i>. - Hx of dental procedure is HY precipitating event, where inoculation of blood occurs via oral cavity → previously abnormal valve gets seeded.
Random points	<ul style="list-style-type: none"> - New-onset murmur + fever = endocarditis till proven otherwise on USMLE. - Reactive thrombocytosis (i.e., high platelets) can occur due to infection. This is not unique to endocarditis, but it is to my observation USMLE likes endocarditis as a notable etiology for it. In other words, if you get an endocarditis question and you're like, "Why the fuck are platelets 900,000?" (NR 150-450,000), don't be confused. - Hematuria can occur from vegetations that launch off to the kidney. - Endocarditis + stroke-like episode (i.e., focal neurologic signs) = septic embolus, where a vegetation has launched off to the brain. - Janeway lesions, Osler nodes, splinter hemorrhages, etc., are low-yield for USMLE and mainly just school of medicine talking points. - HACEK organisms nonexistent on USMLE.
Management	<ul style="list-style-type: none"> - Blood cultures <i>before</i> antibiotics is important for 2CK. - Transesophageal echocardiography (TEE) confirms diagnosis after blood cultures. Transthoracic echocardiography (TTE) is not done for endocarditis. - For 2CK, empiric treatment for endocarditis is vancomycin, PLUS either gentamicin or ampicillin/sulbactam. - Vancomycin targets gram-positives (including MRSA). Gentamicin targets gram-negatives. - Endocarditis prophylaxis given prior to a dental procedure is usually ampicillin or a second-generation cephalosporin, such as cefoxitin. - Indications for endocarditis prophylaxis are: <ol style="list-style-type: none"> 1) Hx of endocarditis (obvious); 2) If there is any prosthetic material in the heart whatsoever; 3) If there is any congenital cyanotic heart disease that has not been completely repaired (if it's been completely repaired with prosthetics, give prophylaxis);


	<p>4) Hx of heart transplant with valvular regurgitation of any kind.</p> <ul style="list-style-type: none"> - Highest yield point for USMLE about endocarditis prophylaxis is that mitral valve prolapse (MVP) and valve regurgitations or stenoses are not an indication. In other words, do not give prophylaxis if the patient has MVP, MR, AS, etc. In addition, bicuspid aortic valve is not an indication.
--	--

Rheumatic heart disease (rheumatic fever) HY points	
	<ul style="list-style-type: none"> - <i>Strep pyogenes</i> (Group A Strep) oropharyngeal infection results in production of antibodies against <i>S. pyogenes</i>' M-protein that cross-react with the mitral valve (i.e., molecular mimicry; type II hypersensitivity). - Can occur with the aortic valve in theory, but on USMLE, it is always mitral valve. - Results in mitral regurgitation acutely and mitral stenosis late, as discussed earlier. - Presents as JONES (J♥NES) → Joints (polyarthritis), ♥ Carditis, subcutaneous Nodules, Erythema marginatum (annular, serpent-like rash), Sydenham chorea (autoimmune basal ganglia dysfunction that results in dance-like movements of the limbs). - Cutaneous Group A Strep infections don't cause rheumatic fever, but can still cause PSGN. - Treatment is penicillin.

Conditions confused for cardiac path	
Panic attack	<ul style="list-style-type: none"> - NBME loves trying to make you think this is an MI. - They'll give you young, healthy patient who feels doom / like he or she is going to die. - Sometimes they mention in stem Hx of MI in family as distraction. - They can say patient has mid-systolic click, as discussed earlier, and then they ask for cause of patient's symptoms → answer = panic disorder, not MVP. Student gets confused, but MVP is almost always asymptomatic, where panic attack is clearly cause of the patient effusively hyperventilating. - Treat with benzo.
Orthostasis	<ul style="list-style-type: none"> - Orthostatic hypotension is defined as intravascular fluid depletion causing a drop of systolic BP >20 mmHg and diastolic BP >10 mmHg when going from supine to standing. - Shows up on 2CK IM form as exactly a drop of 20 and 10, respectively, for systolic and diastolic BPs in a patient with fainting → answer = "intravascular fluid depletion." - Diuretic use is big risk factor.
Vasovagal syncope	<ul style="list-style-type: none"> - Fainting in response to stressor (e.g., emotional trigger). - Stress triggers an initial sympathetic response, which in turn triggers a compensatory parasympathetic response. This latter response is excessive in some people, where the peripheral arterioles dilate and the heart slows too much → decreased cerebral perfusion → lightheadedness/fainting. - 2CK wants you to know a tilt-table test can be used to diagnose, where a reproduction of symptoms can occur.
Carotid sinus hypersensitivity	<ul style="list-style-type: none"> - USMLE likes this for both Steps 1 and 2. - They'll say dude was shaving then got lightheadedness or fainted. - Mechanism is ↑ stretch of carotid sinus baroreceptors → ↑ afferent CN IX firing to solitary nucleus of the medulla → ↑ efferent CN X parasympathetic firing down to cardiac nodal tissue → ↓ HR → ↓ CO → ↓ cerebral perfusion.
Costochondritis	<ul style="list-style-type: none"> - Inflammation of cartilage at rib joints. - Will present as chest pain that worsens with palpation or when patient reaches over the head or behind the back. These two findings are clear indicators we have an MSK condition, not cardiac. - Can be idiopathic, caused by strain (e.g., at the gym), or even post-viral.

Pleurodynia	<ul style="list-style-type: none"> - MSK condition asked twice on 2CK material that has nothing to do with the lungs, despite the name. - This is viral infection (Coxsackie B) causing sharp lateral chest pain due to intercostal muscle spasm. Sometimes students choose pericarditis, etc., even though the presentations are completely disparate. - Creatine kinase can be elevated in stem due to ↑ tone of muscle.
Viral pleurisy	<ul style="list-style-type: none"> - Viral infection causing inflammation of the pleura (layers covering the lungs), leading to sharp chest pain. - If this is the answer, CK will be normal (unlike pleurodynia, because it's not MSK).
Diffuse esophageal spasm	<ul style="list-style-type: none"> - Can cause angina-like pain in patient without cardiovascular disease. - I discuss this in detail in the Gastro section.
Gastroesophageal reflux	<ul style="list-style-type: none"> - Can present as chest pain confused for MI. ECG will be normal, clearly. - I discuss GERD in detail in the Gastro section.

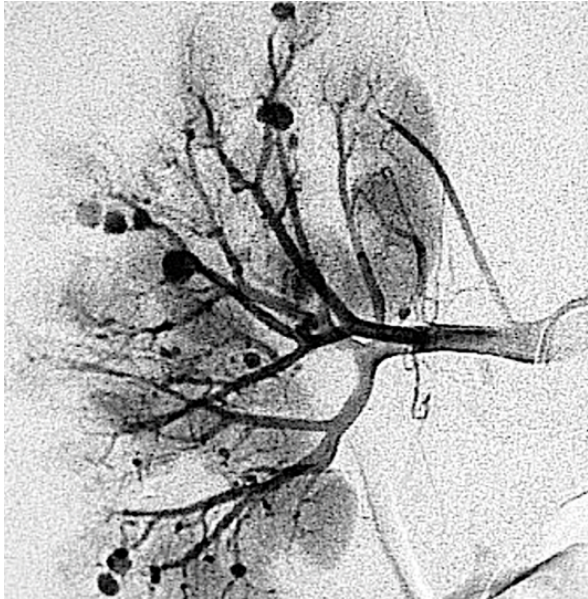
Arterial vs venous disease	
Arterial disease	<ul style="list-style-type: none"> - Caused by atherosclerotic disease; presents as diminished peripheral pulses in patient over 50 who has risk factors, e.g., diabetes, smoking, HTN. - Lower legs can be shiny and glabrous (trophic changes). - Arterial ulcers are small and punched-out; located on tops/bottoms of feet and toes.  <ul style="list-style-type: none"> - Ankle-brachial indices (ABIs) are first step in diagnosis (exceedingly HY on 2CK), which compare BP in ankle to the arm; if <0.9, this reflects ↓ peripheral blood flow due to atherosclerosis. - If ABIs are not listed as first step in diagnosis for whatever reason, choose Doppler ultrasound. There is one 2CK NBME Q where this is the case. - After ABIs, next step is exercise stress test (if listed) in order to determine exercise tolerance. If not listed, go straight to "recommend an exercise / walking program." Do not choose cilostazol first or arteriography as answers. - One NBME form has "prescription for an exercise program" as the answer. Students say, "Why does it say 'prescription'?" No fucking idea. Ok? - Surgery is indicated in the event of critical limb ischemia, which is when there is chronic ischemic rest pain, ulcers, or gangrene. - First surgical intervention is usually angioplasty +/- stenting. Endarterectomy and bypass surgery are indicated for more severe blockages. - All patients with arterial disease should be on triad of 1) ACEi/ARB, 2) statin, 3) anti-platelet therapy (same as carotid stenosis). This is unrelated to the management sequence of exercise program → cilostazol → surgery.

Venous disease	<ul style="list-style-type: none"> - Congestion of venous system usually from valvular incompetence; idiopathic / familial; varicose veins are one type of venous disease and are not synonymous; patients can have venous disease without varicosities. - Peripheral pulses are normal (those reflect arteries, not veins). - Lower legs demonstrate "brawny edema," which is a brown, hemosiderin-laden edema due to ↑ pressure / micro-extravasations; hyperpigmentary changes resulting in brown/red skin is known as stasis dermatitis, aka post-phlebitic syndrome; the latter is a term is asked on 2CK, so know the annoying vocab. - Venous ulcers are large and sloughy, and located at the malleoli.  <ul style="list-style-type: none"> - Diagnose with venous duplex ultrasonography of the legs; first treatment is compression stockings. Never choose answers such as venous stripping or glue agents, etc. - Venous disease ↑ risk for DVT and superficial thrombophlebitis. If patient has active DVT or STP, answer = subcutaneous enoxaparin (heparin) over compression stockings. - Surgery is indicated if there are significant skin changes, venous ulcers, or for symptomatic varicose veins (i.e., pain, itching, swelling, cramps). - You could be aware that sclerotherapy is often chosen as the first surgery, where a sclerosing (scarring) agent is injected into the vein, causing it to close where the blood is re-routed to other veins. But basically always, just compression stockings, or rarely heparin for DVT or STP, is the answer.
----------------	---

Cardiac stress test points	
	<ul style="list-style-type: none"> - Most 2CK Qs that ask about stress tests are in the context of evaluating patients for perioperative MI risk. - It is rare the Q will force you to choose between different types of stress tests. 4/5 Qs will just list one stress test, where it is simply assessing, "Do you know a stress test should be done, period, in this scenario." - Stress tests are also done for peripheral arterial disease prior to recommending an exercise/walking program (as mentioned above).
Exercise ECG	<ul style="list-style-type: none"> - Most common stress test. - The answer on USMLE for patients who have stable angina, where you're looking for ST depressions (i.e., evidence of ischemia) with exertion. - Requires a patient has a normal baseline ECG in order to perform. - In other words, the Q will give you a big 15-line paragraph + mention in the last line that the patient's baseline ECG shows, e.g., a LBBB from a year ago that's unchanged. This means ECG stress test is wrong in this situation, since you need to have a normal ECG to

	do it. The 1/5 Qs that force you to choose between stress tests want you to know this detail, basically, where you just choose the non-ECG stress test instead.
Exercise echo	<ul style="list-style-type: none"> - Used to look for heart failure (i.e., ↓ EF) with exertion, not overt ischemia. - In other words, the answer on USMLE for patients who don't get chest pain with exertion (i.e., don't have stable angina), but who get shortness of breath with exertion. This reflects, at a minimum, left heart decompensation with possible ↓ EF. - Also the answer for patients who have abnormal baseline ECG.
Pharmacologic	<ul style="list-style-type: none"> - Refers to numerous answer choices on USMLE – i.e., dobutamine-echo, dipyridamole-thallium. - The answer on USMLE for patients who cannot exercise, such as in the setting of angina when merely walking up a single flight of steps, or in patients imminently undergoing major surgery (e.g., AAA repair), where perioperative MI risk needs to be assessed. I have seen both of these scenarios on 2CK forms. - The USMLE will typically not force you to choose between stress tests. As I mentioned at the top of this table, they will usually just have the pharmacologic stress test as the only one listed. - Dobutamine is a β_1-agonist that stimulates the heart (i.e., ↑ oxygen demand). Echo can then be done to look for ↓ EF (i.e., heart failure). - Dipyridamole is a phosphodiesterase inhibitor that dilates arterioles. HR goes up to compensate, thereby ↑ myocardial oxygen demand. Thallium is then used to look at perfusion of the myocardium.
Cardiac scintigraphy	<ul style="list-style-type: none"> - "Cardiac scintigraphy" is a broad term that refers to any evaluation of the heart in which some form of radiotracer is used (i.e., thallium, technetium, sestamibi). - This is the same as pharmacologic stress test for all intents and purposes on USMLE, even though technically it need not require myocardium is stimulated and can just be used to look at blood flow to the heart in the resting state. - The point is: This is an answer on 2CK sometimes as just another way of them writing "pharmacologic stress test." Choose it if the patient cannot exercise.
Myocardial perfusion scan	<ul style="list-style-type: none"> - "Myocardial perfusion scan" is one type of cardiac scintigraphy that evaluates blood flow to myocardium. It is non-invasive, whereas coronary angiography is invasive and evaluates coronary blood flow via the use of a catheter. - This is interchangeable with cardiac scintigraphy and pharmacologic stress test on USMLE for all intents and purposes.

Knee trauma causing popliteal arterial injury	
Knee dislocation	<ul style="list-style-type: none"> - If Q gives you MVA where the knee is injured + absent pulses distally, the sequence of answers they want is knee relocation first, followed by arteriography to look for popliteal artery injury. - In one of the 2CK Qs, they already tell you the knee is relocated, then the answer is "arteriography with runoff." Students say, "what's the runoff part?" No fucking idea, it's just what they want.
Penetrating trauma	<ul style="list-style-type: none"> - If Q gives gunshot wound to the knee + absent distal pulses, go straight to "surgical exploration" as the answer. - This could be thought of as the knee-equivalent of a gunshot wound to the abdomen, where straight to laparotomy (even if patient is stable) is the answer.

HY Vasculitides (fancy word that's pleural for vasculitis)	
Granulomatosis with polyangiitis	<ul style="list-style-type: none"> - Formerly known as Wegener granulomatosis. - Answer on USMLE for adult with triad of 1) hematuria, 2) hemoptysis, and 3) "head-itis" – i.e., any problem with the head, such as nasal septal perforation, mastoiditis, sinusitis, otitis. - Associated with cANCA and anti-proteinase 3 (anti-PR3) antibodies. - Causes "necrotizing glomerulonephritis" that can lead to rapidly progressive glomerulonephritis (RPGN).
Eosinophilic granulomatosis with polyangiitis	<ul style="list-style-type: none"> - Formerly known as Churg-Strauss. - Presents as combo of asthma + eosinophilia +/- head-itis. - Head-itis always seen in Wegener vignettes, but maybe only ~50% of CS Qs. - Renal involvement rare for CS. - Associated with pANCA and anti-myeloperoxidase (anti-MPO) antibodies.
Microscopic polyangiitis	<ul style="list-style-type: none"> - Will just present as hematuria in a patient who is pANCA / anti-MPO (+). - Similar to Wegener, can cause RPGN.
<p>- The above three conditions can be associated with a weird neuropathy called mononeuritis multiplex, which means neuropathy of "one large nerve in many locations" – e.g., wrist drop + foot drop in same patient.</p> <p>- You don't need to worry about the fancy term "mononeuritis multiplex," but what I do want you to be aware of is that neuropathy will sometimes show up in these vasculitis vignettes, so don't be confused about it.</p>	
Polyarteritis nodosa (PAN)	<ul style="list-style-type: none"> - Medium-vessel vasculitis that causes a "string of pearls" appearance of the renal vessels.  <ul style="list-style-type: none"> - Causes fibrinoid necrosis, which means it looks like fibrin but it ain't fibrin. - One NBME Q has "segmental ischemic necrosis" as the answer. - Can be caused by hepatitis B. - For whatever reason, USMLE wants you to know PAN spares the lungs – i.e., it does not affect the pulmonary vessels.
Takayasu arteritis	<ul style="list-style-type: none"> - Aka "pulseless disease." Classically affects Asian women 40s or younger. - Inflammation of large vessels, including the aorta. - Always affects the subclavian arteries (which supply the arms), which is why it can cause weakly, or non-palpable, pulse in the upper extremities.
Temporal arteritis	<ul style="list-style-type: none"> - Aka giant cell arteritis. - 9/10 Qs will be painful unilateral headache in patient over 50. I've seen one Q on NBME where it's bilateral. - Flares can be associated with low-grade fever and high ESR.

	<ul style="list-style-type: none"> - Patients can get proximal muscle pain and stiffness. This is polymyalgia rheumatica (PMR). The two do not always go together, but the association is HY. (Do not confuse PMR with polymyositis. The latter will present with ↑ CK and/or proximal muscle weakness <i>on physical exam</i>. PMR won't have either of these findings. I talk about this stuff in detail my MSK notes.) - Patients can get pain with chewing. This is jaw claudication (pain with chewing). - Highest yield point is we give steroids before biopsy in order to prevent blindness. - An NBME has "ischemic optic neuropathy" as the answer for what complication we're trying to prevent by giving steroids in temporal arteritis. - IV methylprednisolone is typically the steroid given, since it's faster than oral prednisone. - It's to my observation many 2CK NBME Qs will give the answer as something like, "Steroids now and then biopsy within 3 days," or "IV methylprednisolone and biopsy within a week." Students ask about the time frames, but for whatever reason USMLE will give scattered/varied answers like that. - Another 2CK Q gives easy vignette of temporal arteritis and then asks next best step in diagnosis → answer = biopsy. Steroids aren't part of the answer. Makes sense, since they're asking for a diagnostic step.
Thromboangiitis obliterans	<ul style="list-style-type: none"> - Aka Buerger disease; technically a vasculitis. - Dry gangrene of the fingers or toes seen generally in male over 30 who's a heavy smoker. - Treatment is smoking cessation. - Don't confuse with Berger disease, which is IgA nephropathy.
Ascending aortitis	<ul style="list-style-type: none"> - Tertiary syphilis can cause ascending aortitis + aortic aneurysm. - Causes "tree-barking" of the aorta.

Thrombophlebitis	
Deep vein thrombosis	<ul style="list-style-type: none"> - DVT will be unilateral thigh or lower leg swelling in patient with risk factors such as: post-surgery, prolonged sedentation, OCP use, Hx of thrombotic disorders (e.g., Factor V Leiden, prothrombin mutation). - Virchow triad for ↑ DVT risk: 1) venous stasis (e.g., post-surgery sedentation), 2) hypercoagulable state (e.g., estrogen use, underlying malignancy), 3) endothelial damage (i.e., smoking). - OCPs contraindicated in smokers over 35 because estrogen causes hypercoagulable state for two reasons: 1) estrogen upregulates fibrinogen; 2) estrogen upregulates factors Va and VIIIa. - USMLE loves nephrotic syndrome as cause of DVT (loss of antithrombin III in the urine → hypercoagulable state). - Antiphospholipid syndrome → DVTs despite paradoxical ↑ PTT (i.e., if PTT is high, you'd think you have bleeding diathesis, not thromboses); may or may not be due to SLE. Antibodies against phospholipids cause <i>in vivo</i> clumping of platelets + ↑ clot initiation, but disruption of <i>in vitro</i> PTT assay means ↑ PTT. - Major danger is DVT can embolize to lungs causing PE → acute-onset shortness of breath and tachycardia + death if saddle embolus. - Homan sign can mean DVT, which is pain in the calf with dorsiflexion of foot. - Diagnose DVT with duplex venous ultrasound of the leg/calf. - Treatment is heparin. - Harder stuff for 2CK is that they care about prophylactic vs therapeutic doses of heparin. Prophylactic dose is lower-dose and is used perioperatively in patients with venous disease/stasis or who are high risk. If a patient has an actual full-blown DVT, however, give therapeutic dose, which is higher-dose.

	<ul style="list-style-type: none"> - There are two 2CK Qs on this stuff. One just mentions a guy going into surgery who has Hx of venous stasis → answer = “prophylactic heparin dose”; “therapeutic heparin dose” is wrong answer. - The second question gives a guy <i>who’s already on prophylactic heparin</i> but gets a DVT anyway. The answer is then “heparin.” It’s weird because students are like, “Wait what? He’s already on heparin though.” And I’m like, yeah, but what they mean is, we have to give therapeutic dose now for the active DVT, which is higher dose. - DVT can rarely cause stroke if an ASD is present (paradoxical embolus). Dumb and low-yield, but it shows up, and students get fanatical over it.
Post-op migratory	<ul style="list-style-type: none"> - Thrombophlebitis means inflammation of a vein. - Post-surgery, this is usually due to changes in hemostasis and coagulability. - Will present as pink/red painful lesions appearing asymmetrically on the limbs within days of surgery. You just need to be able to diagnose this.
Trousseau sign of malignancy	<ul style="list-style-type: none"> - Migratory thrombophlebitis classically due to head of pancreas adenocarcinoma. But this can also be seen with adenocarcinomas in general, e.g., pulmonary.
Catheter-associated septic thrombophlebitis (CAST)	<ul style="list-style-type: none"> - Shows up on 2CK form as patient who had a catheter in and then develops a 4-cm indurated, painful, fluctuant cord in his arm (refers to vein). - Answer = “excision of vein.” Obscure question, but not my opinion. Take it up with NBME if you think it’s weird.
Pelvic septic thrombophlebitis (PST)	<p>The answer on USMLE in a woman who has post-partum endometritis (fever + tender lower abdomen) with persistent fever >48 hours despite antibiotics.”</p> <ul style="list-style-type: none"> - Endometritis can lead to ↑ risk of local infective clots in the ovarian veins. - If they give you a post-partum woman with sepsis (i.e., SIRS + infection), but the vignette doesn’t fit PST as described above, the answer is “puerperal sepsis” on the 2CK form. The latter is a more general term and can refer to many causes of post-partum sepsis (including PST confusingly enough).
Superficial thrombophlebitis	<ul style="list-style-type: none"> - Painful palpable cord in the ankle that may or may not track up to the knee. - Seen in patients with venous insufficiency. - Answer is “subcutaneous enoxaparin.” Compression stockings are typically the answer for first step in venous insufficiency, but if you have an active ST or DVT, heparin must be given as first step. - There will occasionally be some intentional redundancy on my end with things I write in this doc if I believe they’re HY enough (as with this).

HY familial dyslipidemias for IM		
Condition	Mechanism	HY point(s)
Hyperchylomicronemia (AR)	Deficiency of lipoprotein lipase or Apolipoprotein C-II	<ul style="list-style-type: none"> - ↑ chylomicrons + TGAs. - Pancreatitis (abdo, not chest, pain). - Xanthomas. - Plasma appears “creamy”.
Hypercholesterolemia (AD)	Deficiency (heterozygous) or absence (homozygous) of LDL receptor or Apo B-100	<ul style="list-style-type: none"> - ↑ LDL. - LDL usually 3-400 in heterozygotes, with MI/death in 30-40s (answer = deficiency of functional LDL receptor). - LDL usually 700-1000 in homozygotes, with MI in teens (answer = absence of functional LDL receptor). - Xanthomas.
Hypertriglyceridemia (AD)	↑ Hepatic production of VLDL	<ul style="list-style-type: none"> - ↑ TGAs. - Pancreatitis.

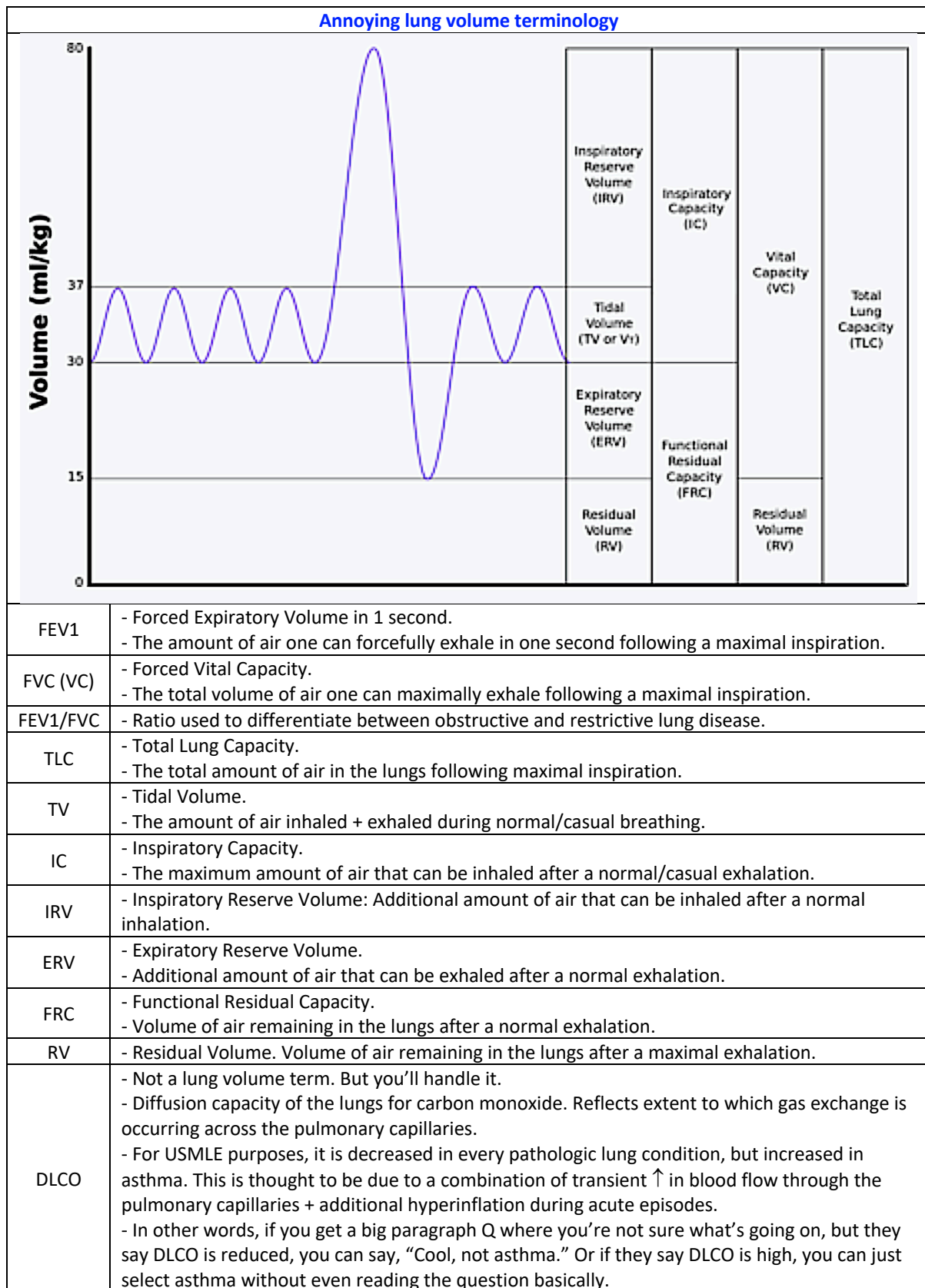
Random HY cardio pharm points	
Verapamil	<ul style="list-style-type: none"> - Non-dihydropyridine calcium channel blocker (acts on nodal calcium channels). - Causes constipation. - Used for AF for rate control sometimes in place of metoprolol (don't worry about the use-case; USMLE doesn't give a fuck; just know MOA and side-effect).
Nifedipine	<ul style="list-style-type: none"> - Dihydropyridine calcium channel blocker (acts on arteriolar calcium channels → dilates arterioles → ↓ peripheral vascular resistance → ↓ BP). - Causes peripheral edema / fluid retention (HY on Family Med). - Used for essential HTN in patients without diabetes, atherosclerotic disease, or renal disease (if that sounds confusing, I talk about this in extensive detail in my HY Risk Factors PDF).
β-blockers	<ul style="list-style-type: none"> - Beta-1 is on myocardium. - Beta-2 is on peripheral arterioles. - There are other binding spots, but the above are what USMLE cares about 99%. - Beta-1-selective blockers follow the mnemonic: A BEAM of beta-blockers: Atenolol, Bisoprolol, Esmolol, Acebutolol, Metoprolol. - The important beta-1/2-non-selective blocker is propranolol. - Labetalol and carvedilol antagonize both beta-1 and alpha-1. They don't end in -olol, which makes them easier to remember/group this way. - Beta-1 antagonism slows HR → ↑ diastolic filling time → ↑ LVEDV. Even though ↑ preload ↑ oxygen demand, the ↓ chronotropy and inotropy cause a ↓↓ in oxygen demand, where the net effect is ↓ oxygen demand. - Step 1 NBME wants beta-blockers as "slowing the rate of diastolic depolarization." In other words, if HR slows, then fractionally more time is spent in diastole, which means the process of returning to systole is delayed/protracted. - Labetalol used first-line in patients who have aortic dissection and traumatic rupture of the aorta. Nitroprusside comes after. - 2CK Q gives "esmolol + nitroprusside" as answer to a traumatic rupture Q, but almost always, they will just want "labetalol." - Timolol can be used topically for glaucoma (↓ aqueous humor production). - Propranolol used for innumerable things → Tx of tachycardia in hyperthyroidism (because also has additional effect of ↓ peripheral conversion of T4 → T3); akathisia (restlessness as an extra-pyramidal side-effect of antipsychotics); essential, alcoholic, or idiopathic tremors (have seen various tremors treated on NBME forms this way, not just essential tremor); social phobia (if patient has asthma, 2CK Psych form wants benzo instead); HOCM (↓ HR → ↑ LVEDV → ↓ murmur/obstruction). - For propranolol, USMLE wants: ↑ LVEDV; ↓ CO, ↑ peripheral vascular resistance. - Propranolol is β1/2-non-selective; β2 agonism normally has dilatory effect on peripheral arterioles, so if we antagonize → ↑ peripheral vascular resistance. - For labetalol, USMLE wants: ↑ LVEDV; ↓ CO, ↓ peripheral vascular resistance. - Labetalol, in contrast, has some α1 blockade effect in addition to β1, so PVR is ↓. - Beta-blocker given after ACEi/ARB in Tx of heart failure (i.e., choose ACEi or ARB first). - Metoprolol used for rate-control in AF. - Beta-blockers can cause depression and sexual dysfunction. - Avoid in patients with lung disease or history of severe or psychotic depression.
Dobutamine	<ul style="list-style-type: none"> - Beta-1 agonist used in pharmacologic stress testing (i.e., dobutamine-echo).
Amiodarone	<ul style="list-style-type: none"> - Potassium channel blocker. - Can cause TdP, greyish skin discoloration, and thyroiditis. - Used for VT in patients without coma or low BP.
Quinidine	<ul style="list-style-type: none"> - Sodium channel blocker. - Can cause TdP and cinchonism (headache + tinnitus).
Digoxin	<ul style="list-style-type: none"> - Directly blocks myocardial Na⁺/K⁺ ATPase pump → causes indirect inactivation of myocardial Na⁺/Ca²⁺ ATPase → more Ca²⁺ remains in myocardial cell → increased contractility. - Also has parasympathomimetic effect at nodal tissue that slows HR. - In other words, digoxin both slows HR + increases contractility.

	<ul style="list-style-type: none"> - Hypokalemia can cause toxicity. This is because digoxin binds to extracellular K^+ binding site, so if less K^+ is around to compete, lower dose is needed to induce effect. - Toxicity presents classically as yellow/wavy "Vincent van Gogh" vision. - Does not decrease mortality in heart failure.
Furosemide	<ul style="list-style-type: none"> - Classic loop diuretic that inhibits the apical $Na^+/K^+/2Cl^-$ ATPase symporter on the thick ascending limb. Apical means side of urine. Basolateral means side of blood. - Most efficacious diuretic at enabling fluid unloading for pulmonary and peripheral edema. Do not decrease mortality in cardiac patients. - Answer on USMLE for patient with heart failure who has \downarrow O₂ sats who "refuses to lie supine/back on the gurney" because he/she can't breathe. Q might say CXR or exam shows fluid 2/3 up the lung fields. - Application of loops can be confused by students with ACEi/ARB. For instance, the latter are used first-line to \uparrow EF in heart failure even if O₂ sats are low (\downarrow AT-II constrictive effect on arterioles \rightarrow \downarrow afterload \rightarrow heart pumps easier), but loops are first-line if the vignette <i>specifically emphasizes</i> the dyspnea and low O₂ sats of the patient as the focus. - HY point is that they can cause hypokalemia. What USMLE loves to do is tell you a patient is initiated on furosemide but it is insufficient + now needs a second diuretic \rightarrow answer = anything that is potassium-sparing (i.e., ENaC inhibitor such as amiloride or triamterene; or aldosterone receptor antagonist such as spironolactone or eplerenone). - Can also cause ototoxicity (tinnitus, vertigo). - Loops \uparrow urinary calcium. This is in contrast to thiazides, which \downarrow it. - Ethacrynic acid is another loop you can be aware of. It is used in patients with sulfa allergies, since furosemide is a sulfa drug. It is also ototoxic.
Thiazides	<ul style="list-style-type: none"> - Hydrochlorothiazide (HCTZ) is HY example; chlorthalidone is "thiazide-like." - Inhibit the Na^+/Cl^- symporter on the apical membrane of the early-DCT. - \uparrow calcium reabsorption in the DCT of the kidney. Used to \downarrow recurrence of calcium stones by promoting \uparrow reabsorption of urinary calcium. In turn, they can sometimes cause hypercalcemia. There is an NBME Q where they ask for MOA of HCTZ, where Na^+/Cl^- symporter inhibition isn't listed; answer is just "\uparrow calcium reabsorption." - Thiazides and dihydropyridine calcium channel blockers are used first-line for HTN in patients without any renal or cardiovascular issues. If patient has proteinuria, \uparrow in creatinine or renin, or pre-diabetes or diabetes, ACEi or ARBs are used first. - Can be used in heart failure in patients with diabetic nephropathy who are already on ACEi and β-blocker. Sounds specific, but there's a new 2CK Q that has thiazide as correct over spironolactone in a diabetic. Spironolactone can cause hyperkalemia in patients who have worrisome kidney function. - Thiazides can cause gout (i.e., contraindicated in gout). - Offline NBME 20 wants you to know thiazides can cause galactorrhea (milky discharge from the nipples) via some obscure mechanism. Literature search shows it accounts for ~0.2% of adverse effects of thiazides, but count on NBME to ask it.
Amiloride, Triamterene	<ul style="list-style-type: none"> - ENaC inhibitors \rightarrow block apical sodium channel in cortical collecting duct \rightarrow \downarrow Na^+ reabsorption \rightarrow \downarrow water reabsorption. - These are potassium-sparing, which means they do not \downarrow serum K^+. This is because by inhibiting the apical ENaC channel, they indirectly inhibit the basolateral Na^+/K^+ ATPase \rightarrow \downarrow Na^+ reabsorption + \downarrow K^+ secretion. - The answer on USMLE for a second diuretic given in a patient already on furosemide who needs additional fluid unloading. Be careful however. I've seen one Q where the patient is on furosemide, but the point of the Q is he/she needs HTN control, and the answer is a thiazide, not the ENaC inhibitor. You want to select an ENaC inhibitor specifically if the Q says, "We have a patient who has peripheral/pulmonary edema due to X cause + is already on furosemide; what do we do now?" \rightarrow answer = amiloride or triamterene.
Spironolactone, Eplerenone	<ul style="list-style-type: none"> - Aldosterone receptor antagonists. - By blocking aldosterone receptor, they \downarrow activity of the basolateral Na^+/K^+ ATPase \rightarrow leads to indirect \downarrow activity of apical ENaC \rightarrow \downarrow Na^+ reabsorption \rightarrow \downarrow water reabsorption.

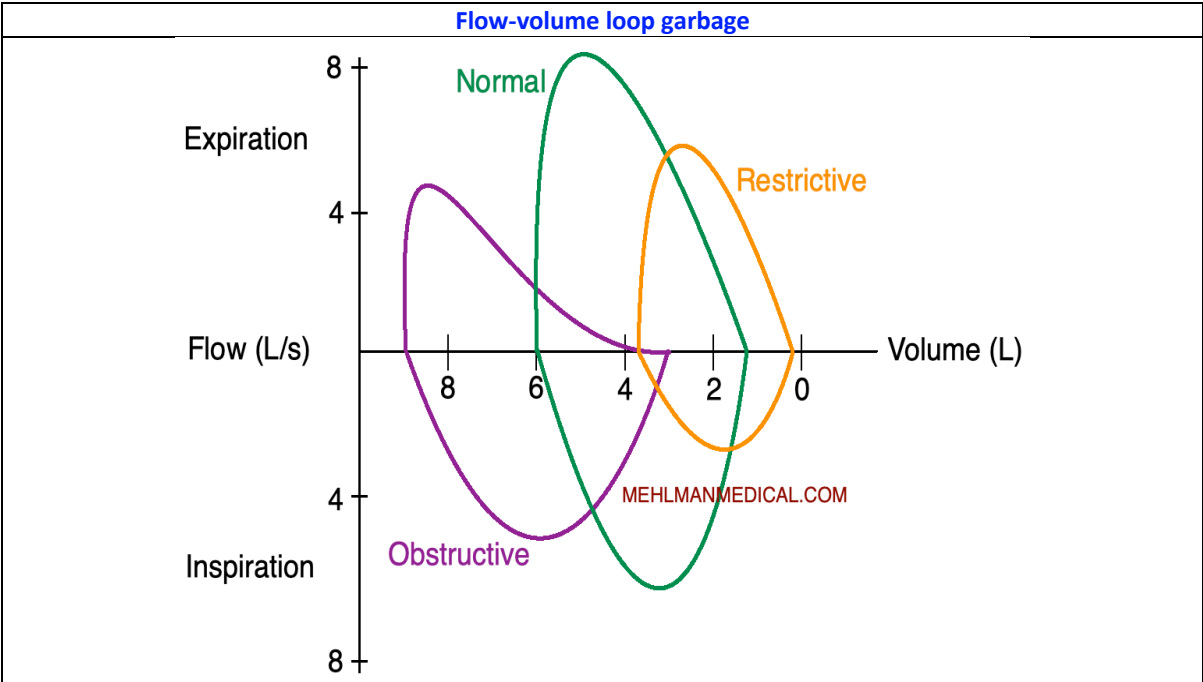
	<ul style="list-style-type: none"> - Potassium-sparing. Same as with ENaC inhibitors, used for fluid unloading in patients who are already on furosemide in whom we worry about dropping their K⁺ too much. - Used in heart failure up the hierarchy of meds – i.e., ACEi/ARB first-line, followed by adding β-blocker, followed by spironolactone (but if patient is diabetic with poor renal function, don't add spironolactone here; give thiazide instead as per new 2CK NBME). - Can be for aldosteronoma (Conn syndrome) prior to surgery. - Spironolactone can cause gynecomastia (anti-androgenic effect by blocking androgen receptors). - Eplerenone has ↓ risk of gynecomastia compared to spironolactone.
Lisinopril	<ul style="list-style-type: none"> - USMLE-favorite ACE inhibitor. - Prevents conversion of AT-I into AT-II in the lungs. - Used for HTN in patients with pre-diabetes, diabetes, atherosclerotic disease, or renal disease (I talk about this in HY Risk Factors PDF in more detail). - Can cause dry cough (ACE is aka bradykininase, so ACEi cause ↓ breakdown of bradykinin in lungs → cough). - Can ↑ serum K⁺, since ↓ aldosterone synthesis. Aldosterone normally secretes K⁺ in the distal kidney). - Avoid in hereditary angioedema.
Valsartan	<ul style="list-style-type: none"> - Angiotensin II receptor blocker (ARB). - Use-cases are identical on USMLE to ACEi (i.e., if you see both as answer choices to a question, they're usually both wrong because they're the "same"). - Doesn't cause dry cough the way ACEi do.
Oxymetazoline, Phenylephrine	<ul style="list-style-type: none"> - α1 agonists → constrict arterioles → ↑ BP → HR ↓ due to baroreceptor reflex. - Highest yield uses on USMLE are for nasal decongestion → constrict capillaries within nasal mucosa → ↓ inflammation → relief of congestion. - Can cause rhinitis medicamentosa, which means rebound nasal congestion upon withdrawal if used non-stop for ~5 days. In other words, patients should use only as needed for a maximum of about ~3-4 days while sick.
Isoproterenol	<ul style="list-style-type: none"> - β1/2 agonist → increases HR and decreases peripheral vascular resistance.
Methyldopa, Clonidine	<ul style="list-style-type: none"> - α2 agonists → prevent presynaptic release of neurotransmitters, especially NE and S. - Methyldopa used for HTN in pregnancy (nifedipine and labetalol also used). - Clonidine used for various psych treatments (e.g., Tourette).
Mirtazapine	<ul style="list-style-type: none"> - α2 antagonist. - Used to treat depression in patients who have anorexia (stimulates appetite).
Ritodrine	<ul style="list-style-type: none"> - β2 agonist used as tocolytic (i.e., slows/delays labor).
Hydralazine	<ul style="list-style-type: none"> - Dilates arterioles → ↓ BP → HR goes ↑ to compensate. - Used for hypertensive emergencies in pregnancy. - Affects calcium currents (but not a calcium channel blocker).
Nitrates	<ul style="list-style-type: none"> - As discussed earlier, they liberate NO which ↑ guanylyl cyclase → ↑ cGMP → relaxation of venous smooth muscle → venous dilation/pooling → ↓ preload on heart → ↓ oxygen demand → relief of anginal pain. - Don't combine with PDE-5 inhibitors (e.g., sildenafil), which prevent breakdown of cGMP. This can lead to severe hypotension. - Combination of hydralazine + nitrates decreases mortality in heart failure. - For sodium nitroprusside, choose arterioles as site of action.
Statins	<ul style="list-style-type: none"> - Statins have 2 HY MOAs on USMLE: 1) inhibit HMG-CoA reductase; 2) upregulate LDL receptors on hepatocytes. - Can cause myopathy and toxic hepatitis. An offline NBME has myopathy as correct over toxic hepatitis. - Indications for statins on 2CK vary depending on the source (i.e., whether to use the 70 vs 100 mg/dL cutoff in certain scenarios), but for IM, give if: <ul style="list-style-type: none"> - Age 20-39 if LDL > 190 mg/dL. - Age 40-75 if LDL > 100 mg/dL. - Age 20-75 in diabetic if LDL > 100 mg/dL.

	<ul style="list-style-type: none"> - Some sources use 70, rather than 100, for the latter two cutoffs. What I can say is that I've seen 2CK NBME Qs where they use 100 as the cutoff (i.e., they give an LDL of 95 and statin is wrong, implying LDL is satisfactory). - Some sources incorporate a CVD risk % of >7.5%, which is more of a moot / pedantic talking point. I've seen one 2CK NBME Q where a CVD risk % shows up in the stem, but it doesn't rely on you knowing that point to get it right.
Fibrates	<ul style="list-style-type: none"> - Fibrates (e.g., fenofibrate) upregulate PPAR-α and lipoprotein lipase; best drugs to decrease triglycerides. - Give if triglycerides >300 mg/dL. - Can cause myopathy and hepatotoxicity, as well as cholesterol gall stones. - If the USMLE asks you why statins + fibrates combined have \uparrow chance of myopathy, the answer is "P-450 interaction."
Ezetimibe	<ul style="list-style-type: none"> - Blocks cholesterol absorption in the small bowel, thereby \downarrow LDL. - USMLE just wants you to know MOA. - Doesn't decrease mortality.
Cholestyramine	<ul style="list-style-type: none"> - Bile acid sequestrant. \downarrow LDL. Doesn't \downarrow mortality. - Causes reduced enterohepatic circulation of bile acids at terminal ileum \rightarrow liver must now convert more cholesterol into bile acids in order to replenish them \rightarrow liver pulls cholesterol out of the blood to accomplish this.
Orlistat	<ul style="list-style-type: none"> - Pancreatic lipase inhibitor used for obesity; can cause steatorrhea.
Niacin	<ul style="list-style-type: none"> - Vitamin B3. Two MOAs USMLE wants you to know: 1) \downarrow VLDL export by the liver; 2) \uparrow HDL more than any other medication. - Administration can cause flushing (caused by prostaglandin, so mitigated by aspirin), gout, and insulin resistance. - Deficiency \rightarrow pellagra \rightarrow 3Ds \rightarrow dementia, dermatitis, diarrhea. - Can present as delirium instead of overt dementia (biggest risk factor for delirium is underlying dementia, so old patient with delirium often has underlying cognitive decline); dermatitis will present on USMLE as either hyperpigmentation of the skin of the forearms or Casal necklace.
Procainamide	<ul style="list-style-type: none"> - Sodium channel blocker that can be used in Wolff-Parkinson-White. - Can cause drug-induced lupus with anti-histone antibodies.
Flecainide	<ul style="list-style-type: none"> - Na⁺ channel blocker used as first-line rhythm control in patients fail rate-control for AF. - Patient should have no structural or coronary artery disease. Otherwise use a potassium channel blocker like amiodarone or dofetilide.
Dofetilide, Ibutilide	<ul style="list-style-type: none"> - Potassium channel blockers. - Can cause torsades (asked on NBME).
Omega/fish oils	<ul style="list-style-type: none"> - Decrease triglycerides.
Morphine	<ul style="list-style-type: none"> - 2CK form gives patient who is in pain from surgery despite being on max doses of morphine + they say blood pressure is elevated + ask what is next best step \rightarrow answer = "increase bolus of morphine." Unusual, since they say max dose of morphine already, but 1) we always full treat pain, and 2) explanation for the Q talks about how pain can lead to high BP. - My point here is that just be aware HTN can be caused by pain \rightarrow treating pain can bring down the BP. - Separately, treatment of MI, acute limb ischemia, and sickle crisis usually includes oxygen + morphine. - Answer on NBME exam for how a patient using a self-administering pump develops morphine overdose = "morphine is converted into active metabolites that accumulate." - Otherwise morphine is odd drug for me to put in this table; didn't know where else to put it though.

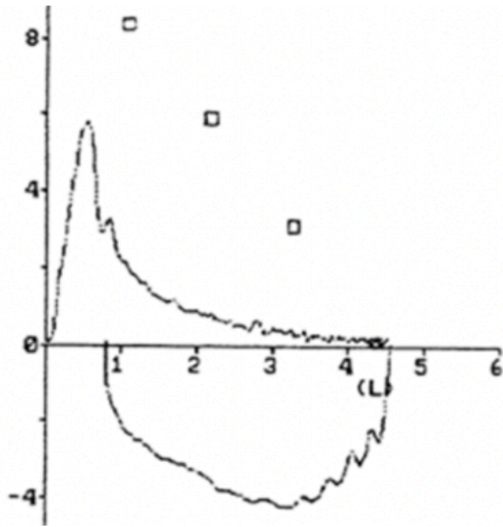
IM Pulmonary



Obstructive vs restrictive lung disease		
	Obstructive Pattern	Normal
	Obstructive Pattern	Restrictive Pattern
	Obstructive	Restrictive
HY conditions	<ul style="list-style-type: none"> - Asthma. - COPD (chronic bronchitis + emphysema). - Old age (i.e., healthy person age 70 vs 20). 	<ul style="list-style-type: none"> - Pulmonary fibrosis due to any cause (i.e., idiopathic; radiation; drugs; autoimmune disease). - Pneumoconioses.
FEV1	↓	↓/↔
FVC	↓	↓
FEV1/FVC	↓ (<70%; normal is 70%)	↑/↔ (>70-80%)
TLC	↑	↓
FVC (VC)	↔/↓	↓
TV	↔	↔/↓
IC	↔/↓	↓
IRV	↔/↓	↓
ERV	↓	↓
FRC	↑ (due to air trapping)	↓ (due to ↓ lung compliance)
RV	↑ (due to air trapping)	↓ (due to ↓ lung compliance)
DLCO	↓ (but ↑ in asthma on USMLE)	↓ (↔ if neuromuscular)
<p>- The reason FEV1/FVC is ↑/↔ in restrictive, as compared to ↓ in obstructive, is because of radial traction, which is a “stickiness” on the outside of the airways (such as from fibrosis) that prevents them from closing as rapidly as in obstructive.</p> <p>- If you feel iffy on lung volumes, a general point to remember is that they’re basically all decreased in restrictive due to ↓ compliance, but various ones are ↑ in obstructive because air can’t get out.</p> <p>- Lifetime inhalation of particulates (i.e., non-smoker simply living in a city) causes an accreted effect on the lungs akin to very slow-onset COPD. So if the USMLE asks for lung volumes in a healthy 70-year-old versus a 20-year-old, select arrows for the former consistent with obstructive lung disease.</p>		



- Don't freak out about the above flow-loops. For USMLE, I'd say the most important point is that you know the expiratory component of the obstructive curve (purple) has a scooped-out/concave shape. This is because obstruction causes the flow rate to be significantly reduced throughout the expiration.



- What USMLE will do is give you a real bootleg Windows 95-type spirometry curve as per above in a 34-year-old + no family Hx + 5-year smoking Hx. You look at curve and say, "No idea what I'm looking at, but top of curve is scooped-out/concave, and I know that means obstructive. So if I'm guessing between COPD or asthma here, which are both obstructive, I'll choose asthma as more likely over COPD in young patient."

	Obstructive	Restrictive
Shape	- Scooped-out/concave appearance.	- Smaller and more symmetric.
Expiratory flow rate	- Airway obstruction causes big reduction in flow rate, which is why it drops precipitously and results in scooped curve.	- Peak expiratory flow rate relatively preserved, but overall size of the loop is reduced due to less volume in the lungs on maximum inspiration.
Inspiratory flow rate	- Less affected compared to expiratory curve. Can be normal or reduced.	- Significantly reduced due to diminished pulmonary compliance.
Volume	- Wider curve, due to increased TLC from air trapping.	- Narrower curve, due to diminished TLC from reduced compliance.

Shunt versus dead space

- When we discuss V/Q mismatch, V = ventilation; Q = perfusion.
 - \downarrow V/Q (ventilation/perfusion) = reduced ventilation relative to perfusion.
 - \uparrow V/Q = reduced perfusion relative to ventilation.
 - **Shunt** = \downarrow V/Q \rightarrow refers to almost all lung conditions on USMLE.
 - **Dead space** = \uparrow V/Q \rightarrow refers to just pulmonary emboli on USMLE.
- If you hear the term “shunt” used in isolation, this refers interchangeably to “pathologic shunt,” where \downarrow V/Q occurs to the point that the patient’s arterial oxygen becomes decompensated. In other words, the reason why a patient has \downarrow O₂ sats is because there’s some sort of lung problem where aeration of the alveoli is \downarrow . But there’s nothing wrong with perfusion (i.e., blood flow isn’t cut off to the lungs).
- \downarrow V/Q can also refer to the physiologic (i.e., normal) shunt we see at the lung bases, where V/Q is 0.6. This is because despite both ventilation and perfusion \uparrow apex \rightarrow base, gravity pulls blood down more greatly than air, so perfusion $\uparrow\uparrow$ toward the bases, whereas ventilation only \uparrow . So V/Q is \downarrow at the bases (shunt).
- Areas of lung with \downarrow V/Q attempt to compensate via hypoxic vasoconstriction, where blood vessels constrict in order to redirect (i.e., shunt) blood to better-ventilated areas. In other words, if an area has low ventilation, constriction of blood vessels in that area lowers Q in order to increase the V/Q ratio and prevent wasting of blood flow.
- If you hear the term “dead space” used in isolation, this refers interchangeably to “pathologic dead space,” where \uparrow V/Q occurs to the point that the patient’s arterial oxygen becomes decompensated. In other words, the reason why a patient has \downarrow O₂ sats is because blood flow is cut off to the lungs. This will be PE (and air, fat, amniotic fluid emboli) on USMLE because the clot that embolizes to the pulmonary arteries compromises blood flow to the pulmonary tissue.
- \uparrow V/Q can also refer to dead space processes that are non-pathologic:
- *Alveolar* dead space = natural, physiologic \uparrow V/Q within the alveoli, where some areas of lung receive more ventilation than perfusion – i.e., the apices (V/Q of \sim 3.0) compared to the bases (\sim 0.6). This is because gravity pulls blood down more than air, so at the apices of the lungs, there’s relatively less blood flow in comparison to how much those areas are ventilated.
 - *Anatomic* dead space refers to parts of the respiratory tree that are naturally ventilated but do not partake in gas exchange, such as the trachea, bronchi, and terminal bronchioles. These areas do not receive perfusion where gas exchange occurs for respiratory purposes, despite being ventilated by air moving in and out.
 - *Physiologic* dead space is the sum of anatomic and alveolar dead space.
- To understand shunt vs dead space better, both involve a right-to-left mixing of deoxygenated blood (right) with oxygenated blood (left). Shunt is a R-to-L mixing where “R” is created by areas of alveoli not receiving enough oxygen; dead space is a R-to-L mixing where “R” is due to \downarrow perfusion to areas of lung.
- An area of lung under-ventilated or -perfused could be said to represent a “zero” in terms of the oxygenation it contributes to the blood. That zero is mixed in with all of the other areas of normal lung. This means *the average* of all areas of lung cannot achieve normal oxygenation because that zero is mixed in. This is why arterial O₂ will be decreased when we have pathologic shunt or dead space.
- In both pathologic shunts (e.g., COPD, pneumonia, asthma) and dead space (PE), there are still areas of lung that have normal V/Q. Administering oxygen to these patients will have differing effect, where shunt is less effectively remedied often due to the extent of hypoxic vasoconstriction, which causes a high fraction of blood to bypass normal V/Q areas altogether, even though a small fraction is diverted appropriately to them. The net result is oxygen administration still fails to increase PaO₂ in shunt. In dead space, where hypoxic vasoconstriction doesn’t occur because ventilation is normal, administered oxygen to normal V/Q areas helps because it comes into contact with more blood overall.
- This can essentially be simplified as: dead space by definition is a *primary* \downarrow in perfusion; shunt causes a *secondary* \downarrow in perfusion. But we don’t call the secondary \downarrow in perfusion “dead space.” Hypoxic vasoconstriction due to shunt is a mere compensatory response to \downarrow ventilation, but it happens to be the case that the blood that is shunted away from the lungs can be greater in volume than the primary \downarrow in perfusion in the setting of a pathologic dead space.

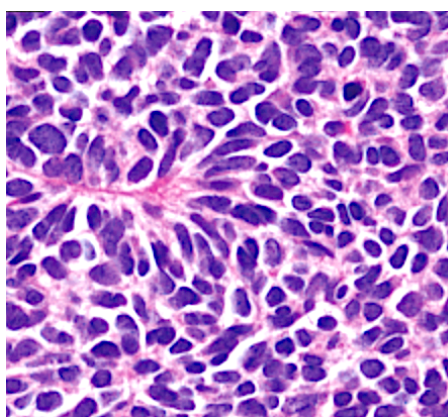
Alveolar-arterial (A-a) gradient stuff

- A is alveolar oxygen; a is arterial oxygen.
- In settings where the patient's arterial oxygen is low, the A-a gradient (normally 5-10 mmHg) tells us whether there's an actual lung pathology or if the patient is merely hypoventilating. In other words,
- **↑ A-a gradient = the lungs are fucked up** = the patient is breathing normally but there is a problem such as impediment of gas exchange, poor lung compliance, or pathologic shunt or dead space. The patient has low arterial oxygen despite sufficient respirations, where alveolar pO₂ is normal in unaffected areas of lung. The normal "A" in unaffected areas of lung minus the low "a" in the blood makes A-a high.
- **Normal A-a gradient = the lungs are normal** = patient is just not breathing enough – i.e., quality and/or quantity of respirations is insufficient. This refers to **opioids, heroin, benzos, and barbiturates** because these agents cause respiratory depression. Normal A-a gradient is also sometimes seen in patients on ventilators. The patient has low arterial oxygen merely because of insufficient respirations, where alveolar oxygen is low throughout the lungs. The low "A" throughout the lungs is due to poor respirations, minus the low "a" in the blood, making A-a not elevated.
- The NBME doesn't expect you to know the exact numbers for A-a gradients. The Q might give you answer choices where A-a gradient is either 40 or 10, where you have to say, "Well clearly the answers with 40 are high and the ones with 10 are normal." So if the Q is a patient who has opioid toxicity with low O₂ sats, you'd select the answer choice with 10 for A-a rather than 40. Not dramatic.
- USMLE also wants you to know that the mechanism for a patient's hypoxemia in pulmonary edema is "high A-a gradient"; this makes sense, as the transudate in the alveolar spaces impedes gas exchange, but the patient's respirations are otherwise fine.
- Old age in healthy persons causes: ↑ A-a gradient, ↓ arterial pO₂, ↑ TLC. This combo is answer on NBME – i.e., even if people are non-smokers, as we live out life inhaling particulates from car exhaust, etc., the lungs experience obstructive changes with age (essentially "very slow COPD").
- Choose normal A-a gradient in patients on ventilators who have ↑ pCO₂. The latter tells us the arterial pO₂ is low because of insufficient respirations.
- My biggest advice is to not automatically assume "high A-a gradient" for every scenario of low O₂ sats. The mistake I see students make is they just think "any issue causing low O₂ sats = A-a gradient must be high."

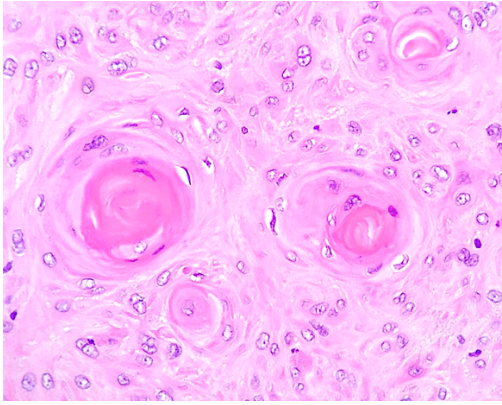

HY pulmonary / respiratory tract cancers for IM


Small cell
bronchogenic
carcinoma

- Small basophilic (purple) cells. NBME can describe these cancer cells as "twice the size of lymphocytes."

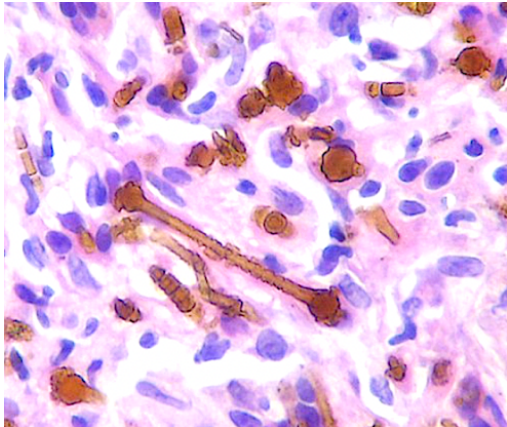


- Occurs centrally in the lung (i.e., hilar / medially). Smoking biggest risk factor.
- Paraneoplastic syndromes exceedingly HY: 1) SIADH (ADH secretion); 2) Cushing syndrome due to ACTH secretion; 3) Lambert-Eaton syndrome (production of antibodies against presynaptic voltage-gated calcium channels); 4) Cerebellar dysfunction / ataxia (anti-Hu/-Yo antibodies).
- Treatment on 2CK is "chemotherapy." Do not do surgery. I believe this is the only time I've seen straight-up "chemotherapy" as correct answer on NBME.

<p>Squamous cell carcinoma</p>	<ul style="list-style-type: none"> - Stains positive for keratin; may have keratin pearls on histo (pink circles).  <ul style="list-style-type: none"> - Similar to small cell, occurs centrally in the lung (i.e., hilar / medially). Smoking biggest risk factor. In other words, the two cancers that start with an “ssss” sound for “central” (i.e., Small cell and Squamous cell) are Central. - Can cavitate → if USMLE gives you lung cancer with a cavitation (i.e., cavity/hole), the answer is squamous cell.  <ul style="list-style-type: none"> - Highest yield point is that it secretes PTHrp (parathyroid hormone-related peptide). This acts like PTH and increases calcium / decreases phosphate, but this is not the same as PTH. Endogenous PTH is <i>suppressed</i> due to negative feedback from high calcium. In other words, choose a down arrow for PTH in squamous cell carcinoma of the lung.
<p>Adenocarcinoma of the lung</p>	<ul style="list-style-type: none"> - Adenocarcinoma means cancer of glands. If the Q says something about biopsy showing glandular morphology, you know they’re talking about adenocarcinoma. - The answer on USMLE for lung cancer in a non-smoker; classically “female non-smokers,” but I’ve seen NBME Qs with this in men. - Normal ground/Earth radiation due to radon is accepted cause of lung cancer in non-smokers. There is NBME Q where they mention non-smoker living in a basement and develops lung cancer. The correlation is probably nonsense in real life, but it’s in an NBME question somewhere. - Does not occur centrally on NBME exam, unlike small cell and squamous, and hence will be described as apical or peripheral lung lesion in non-smokers. - Apical tumors can be known as Pancoast tumors and cause Horner syndrome (miosis, ptosis, anhidrosis) due to impingement on C8 superior cervical ganglia (sympathetic nerves). They can also cause SVC syndrome (flushing of the face + congestion of neck veins) or brachiocephalic syndrome (only right side of

	<p>face/neck) due to impingement on venous return. (+) Pemberton sign is worsening of flushing + neck vein congestion when raising the arms above the head.</p> <ul style="list-style-type: none"> - Can be associated with migratory thrombophlebitis (Trousseau sign of malignancy). The latter is not limited to head of pancreas cancer. Adenocarcinomas in general are known to be associated with hypercoagulable state due to malignancy. USMLE won't ask specific mechanism, but liberation of tissue factor (factor III) by these cancers is a proposed etiology. - Associated with hypertrophic osteoarthropathy (clubbing + hand pain due to lung cancer); mechanism is fibrovascular proliferation. Literature says adenocarcinoma of lung is most common cause, although the association isn't 100% specific.
Large cell carcinoma	<ul style="list-style-type: none"> - Nonexistent lung cancer on USMLE. Bogus/garbage diagnosis. I don't think I've ever seen this assessed.
Bronchogenic carcinoid tumor	<ul style="list-style-type: none"> - Pulmonary nodule that secretes serotonin or serotonin-like derivatives, resulting in carcinoid syndrome (i.e., tachycardia, flushing, diarrhea). - A type of neuroendocrine tumor. - Carcinoid tumors are classically appendiceal and of the small bowel, but you should be aware that bronchogenic carcinoids exist. - USMLE wants urinary 5-hydroxy indole acetic acid (5-HIAA) for initial step in Dx.
Mesothelioma	<ul style="list-style-type: none"> - Cancer of "mesothelial cells" (answer on NBME) seen in patients with prior occupational exposure to asbestos. - Asbestosis occurs first, which then gives rise to mesothelioma years later. - Shipyard and construction workers are buzzy for prior occupational exposure. - Asbestosis will be described as pleural or supradiaphragmatic plaques ("soft tissue plaques seen on CXR"). Pulmonary biopsy shows ferruginous bodies. - Calretinin (+); a protein that is highly indicative of mesothelioma on staining. - Mesothelioma appears as a whiteish cancer and is described as an "encasing rind of pleural-based tumor" (i.e., circumferentially surrounds/wraps around the lungs). 
Nasopharyngeal carcinoma	<ul style="list-style-type: none"> - Can be caused by EBV. - A type of squamous cell carcinoma of the airway.
Laryngeal cancer	<ul style="list-style-type: none"> - Squamous cell carcinoma of vocal cords. - Smoking is major risk factor. - New NBME Q wants you to know this spreads to cervical lymph nodes.
Laryngeal papillomatosis	<ul style="list-style-type: none"> - Pediatric condition characterized by warts of the vocal cords. - Lesions will have papillary structures on biopsy. - Due to HPV 6/11 exposure from maternal vaginal canal.

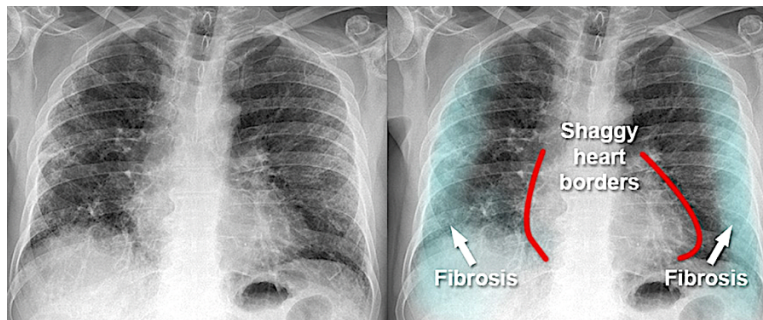


Pneumoconioses for IM	
Asbestosis	<p>- As already mentioned above in the mesothelioma section, this is associated with shipyard workers, construction workers, and electricians. It can give rise to mesothelioma later in life.</p>  <p>- The above ferruginous body is dumbbell-shape. Choose macrophage as the answer on USMLE for the cell that initiates pulmonary fibrosis (in response to asbestos and in general).</p> <p>- Causes restrictive lung pattern.</p>
Berylliosis	<p>- Occupational exposure to beryllium in the aerospace / aeronautical industry.</p> <p>- Causes restrictive lung pattern.</p> <p>- Can cause granulomas.</p>
Silicosis	<p>- Occupational exposure to silicon (sand) in foundry or stone quarry workers.</p> <p>- Can cause egg-shelf calcifications in upper lobes.</p> <p>- Increases risk of tuberculosis infections.</p> <p>- Avoid anti-TNF-α agents (i.e., infliximab, adalimumab, etanercept) in these patients due to increased TB risk (TNF-α needed to suppress/fight TB).</p>
Anthraco-sis	<p>- Aka "coal miner's lung."</p> <p>- Black discoloration of the lung.</p> <p>- Can be either obstructive or restrictive.</p>
Caplan syndrome	<p>- Rheumatoid arthritis + any pneumonociosis, presenting as pulmonary nodules.</p> <p>- Clinical relevance is that patients with RA are at increased risk for developing pneumoconioses if they have a workplace exposure.</p>

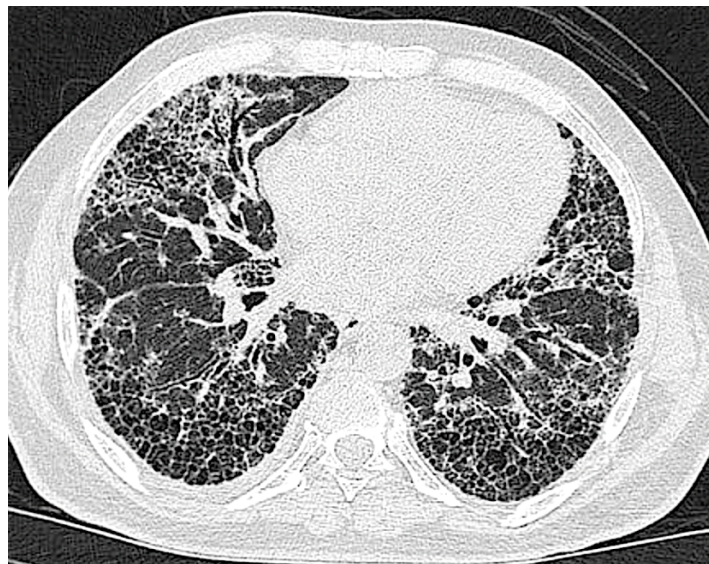
HY General lung conditions for IM

Idiopathic pulmonary fibrosis
(Usual interstitial pneumonitis)

- The answer on USMLE for a patient over the age of 50 who has 6-12+ months of unexplained dry cough. This is how it shows up 4/5 times.
- Textbook restrictive lung disease, with \leftrightarrow or \uparrow FEV1/FVC. The reason for the FEV1/FVC being greater than in obstructive lung disease is radial traction, as mentioned earlier.
- CXR and CT scan show "reticular" or "reticulonodular" pattern. These descriptors are exceedingly HY on USMLE, where students will overlook them in the vignette, but they are hugely buzzy for restrictive lung disease. They are colloquially known as "honeycombing," but I have not seen the USMLE give a fuck about the latter colloquialism. They frequently just say "reticular" and "reticulonodular," and then you know right away, "Boom. Restrictive lung disease," i.e., fibrosis, etc. Tangentially, it's to my observation that NBME will say "reticulogranular" frequently for NRDS, but the two vignettes are clearly disparate anyway.

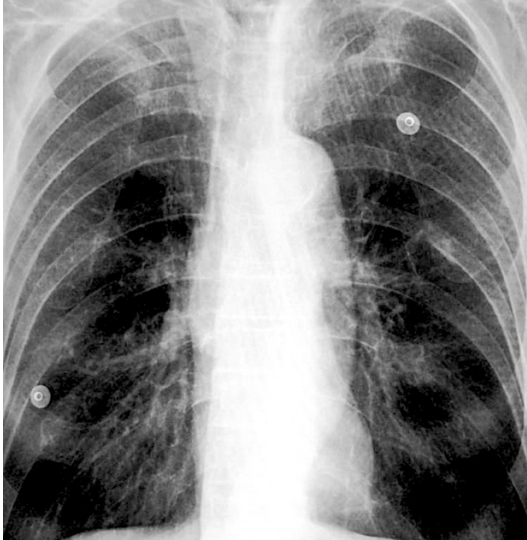


- After the CXR and spirometry are performed, 2CK wants "high-resolution CT of chest" as answer for next best step.



"Honeycombing" = reticular / reticulonodular pattern.

- New 2CK NBME wants "lung biopsy" as answer to confirm diagnosis of interstitial lung disease (i.e., idiopathic pulmonary fibrosis) after imaging.
- Vignette can also mention loud P2 (means pulmonary hypertension) with "dry inspiratory crackles heard bilaterally."
- 1/10 times, the Q will be patient over 50 with increasing fatigue and shortness of breath over 6-12 months, with only 1 month of cough, where it initially sounds like heart failure, and they'll say CXR shows "interstitial markings" instead of reticular/reticulonodular patterning.

	<p>However, they say patient has “↑ FEV1/FVC showing restrictive pattern” in the stem, which gives it away.</p> <ul style="list-style-type: none"> - You need to know that “usual interstitial pneumonitis” (UIP) is another name for idiopathic pulmonary fibrosis. Yes, the name is weird, but it’s not my opinion and it’s asked twice on the NBMEs, where instead of writing “idiopathic pulmonary fibrosis” as the answer, they write “usual interstitial pneumonitis.” UIP is technically a broad term that can refer to many restrictive lung conditions, but as I said, on NBME they use this synonymously with idiopathic pulmonary fibrosis. - Tx on 2CK = pirfenidone → anti-fibrotic agent that inhibits TGF-β-mediated synthesis of collagen.
Chronic obstructive pulmonary disease (COPD)	<ul style="list-style-type: none"> - COPD = chronic bronchitis + emphysema. - Smokers will have combination of the two. When we say a smoker has COPD, we are saying he/she has chronic bronchitis + emphysema at the same time. - The term COPD can in theory apply to any obstructive disease of the lung that is chronic (e.g., asthma, Kartagener, etc.) but when the term is used without any specific condition attached, it refers to the combo of chronic bronchitis and emphysema.  <ul style="list-style-type: none"> - Hyperinflated lungs in COPD (due to air trapping) can push the heart to the midline. NBME will say there’s a “long, narrow cardiac silhouette,” or a “point of maximal impulse palpated in the sub-xiphoid space.” In left ventricular hypertrophy, in contrast, there will be a lateralized apex beat, or a point of maximal impulse in the anterior axillary line. - Home oxygen is indicated on 2CK if O₂ sats are: <ul style="list-style-type: none"> - <88% saturation (55 mm Hg), or - <89% saturation (60 mm Hg) if the patient has cor pulmonale. - First-line Tx is now considered to be a long-acting muscarinic receptor antagonist (i.e., LAMA such as tiotropium) or a long-acting β₂ agonist (i.e., LABA such as olodaterol), either alone or in combination. - If insufficient, add an inhaled corticosteroid (e.g., fluticasone). - Should be noted that a question on an earlier NBME has ipratropium (SAMA) as the answer for 1st-line in COPD, but there aren’t any other anti-muscarinic or β₂ agonists listed. So the point is that if you are forced to choose a SAMA or SABA (i.e., albuterol) on USMLE, these are OK, but newer guidelines say start with a LAMA or LABA. - “Exacerbation of COPD” as a diagnosis on USMLE will always give a patient with <i>high CO₂</i>. This is really important. In other words, if they

	<p>give you a big paragraph and you're not sure of the Dx, if you see CO₂ is not elevated, the answer is not COPD exacerbation.</p> <ul style="list-style-type: none"> - COPD exacerbations can be triggered by minor chest infections, so always give antibiotics on 2CK, even though etiology is usually viral. - Patients with COPD are chronic CO₂ retainers, so they will have a chronic respiratory acidosis (i.e., ↑ CO₂ and ↑ bicarb; pH can either be ↓ or compensated back into normal range). - For 2CK, lung cancer screening with annual low-dose chest CT is done in patients who meet all of the following: <ol style="list-style-type: none"> 1) age 50-80; 2) have 20-pack-year Hx of smoking; and 3) smoked within the past 15 years.
Chronic bronchitis	<ul style="list-style-type: none"> - Chronic bronchitis = productive cough for at least 3 months in a year, for 2+ years. - Reid index >0.5 (ratio of the thickness of bronchial mucous-secreting glands to the bronchial wall itself). <0.4 is considered normal. - Chronic bronchitis is known as "blue bloater" because the mucous sits in the alveolar spaces and impairs gas exchange. This results in a shitload of hypoxic vasoconstriction → patient can become acutely blue and hypoxic during exacerbations. - The hypoxic vasoconstriction of pulmonary vessels causes pulmonary hypertension (i.e., if the vessels constrict, then pressure in the more proximal pulmonary arterioles increases). This increased afterload on the right heart can lead to right ventricular hypertrophy and right heart decompensation. When right heart failure (i.e., evidence of JVD or peripheral edema) occurs due to a pulmonary cause, we now call that cor pulmonale, as discussed in the Cardio PDF. - The pulmonary hypertension can cause a loud P2 and tricuspid regurg prior to cor pulmonale occurring. - Don't confuse chronic bronchitis with acute bronchitis, which can present as a worsening cough in patient (with or without COPD) following a viral infection. This is a temporary irritation/inflammation of the airways that is self-resolving.
Emphysema	<ul style="list-style-type: none"> - Emphysema = loss/destruction of alveolar surface area. - When alveolar surface area is reduced, so is alveolar capillary surface area, since the capillaries are within the alveolar walls → ↓ gas exchange. - Known as "pink puffer," since although gas exchange is impaired, sudden and acute increases in hypoxic vasoconstriction, as with chronic bronchitis, are not a feature. - "Bullous changes" on CXR are synonymous with emphysema on USMLE. - Smokers can get centri-acinar emphysema (proximal alveolar structure is destroyed). - α₁-antitrypsin deficiency patients get pan-acinar emphysema (entire alveolus destroyed).
α ₁ -antitrypsin deficiency	<ul style="list-style-type: none"> - Codominant genetic condition resulting in emphysema and hepatic cirrhosis. - ZZ allele combo is worst and results in disease (asked on USMLE). - α₁-antitrypsin is an enzyme produced by the liver that travels to the lungs and breaks down neutrophilic elastase. Elastase is an enzyme that normally causes damage to the alveoli. Homeostatically, elastase is required in small amounts for normal pulmonary function and cell turnover, but in high amounts it destroys the alveoli, resulting in emphysema. - Vignette will give young adult who has sibling or parent who's had early-onset emphysema or cirrhosis.

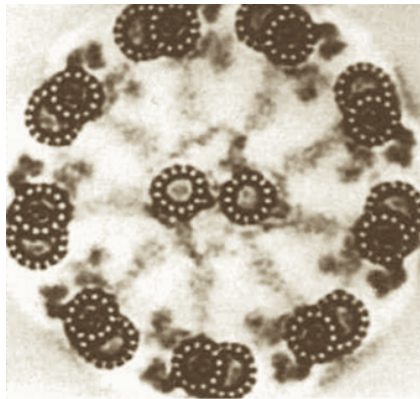
	<p>- The USMLE Q can absolutely say the patient is a smoker or drinks alcohol. For instance, they might say the patient is 34 and has been smoking for 5 years and has bullous changes on CXR, or that the father died from alcoholic cirrhosis, and the student thinks, "Oh that can't be α1-antitrypsin deficiency though because they said smoking/alcohol." But the key point is that this condition <i>increases the risk</i> for early-onset emphysema and cirrhosis. Normally, COPD should take 20+ years of smoking to develop, not 5.</p>
Asthma	<p>- Bronchospasm that occurs either idiopathically/hereditarily, or in response to certain allergens or cold air.</p> <p>- One-third of patients with asthma only present with a dry cough and no problems breathing. This is called cough-variant asthma. It will often present as a patient with a dry cough that's worse in the winter.</p> <p>- Can also present as part of atopy constellation – i.e., dry cough in winter, seasonal allergies / rhinoconjunctivitis / urticaria in spring, and eczema in summer.</p> <p>- Aspirin-induced asthma mechanism HY for USMLE → inhibition of COX by aspirin → shunting of arachidonic acid down lipoxygenase pathway → increased leukotrienes → increased bronchoconstriction.</p> <p>- Samter triad = aspirin allergy, asthma (due to aspirin), nasal polyps.</p> <p>- "Increased expiratory phase" is a buzzy phrase that will be thrown into quite a few asthma vignettes. It is not specific for asthma and can refer to any obstructive pathology, but I just make note of it here because you'll see it quite a bit for asthma and say, "What's that mean?" → in obstructive conditions, it takes us a lot longer to exhale (FEV1 is ↓↓).</p> <p>- Acutely, asthma causes ↓ CO₂, ↑ pH, ↔ bicarb. This is an acute respiratory alkalosis. Even though the patient is having difficulty breathing, CO₂ diffuses quickly, whereas O₂ diffuses slowly, so insofar as the patient's respiratory rate is ↑, CO₂ will be ↓. Bicarb is unchanged because it takes the kidney about a day to alter excretion. In contrast, CO₂ is ↑ in COPD because there is large amounts of hypoxic vasoconstriction due to excessive mucous (chronic bronchitis) or ↓ alveolar surface area, so CO₂ can't get out, even with faster breathing. In asthma, alveolar surface area is intact, and the degree of mucous production and hypoxic vasoconstriction is not nearly as bad as chronic bronchitis.</p> <p>- The combination of ↓ CO₂ and ↓ O₂ in acute asthma attack is known as type I respiratory failure. Eventually, the patient will begin to fatigue and breathing rate will slow. This will be observed as CO₂ and pH rebounding to normal levels <i>despite</i> O₂ remaining low. This means the patient is in transition to a type II respiratory failure (i.e., hypoventilation), where we have ↑ CO₂ and ↓ O₂. USMLE wants intubation as the intervention.</p> <p>- 2CK Q gives vignette of asthma and then asks for best initial step in diagnosis → answer = "spirometry." The expiratory component of the curve, as discussed earlier, will appear concave.</p> <p>- Should be aware methacholine challenge can also be done to diagnose. This is a muscarinic agonist that bronchoconstricts and can induce symptoms. Never give during acute episode. This can be tried between episodes. But if you're forced to choose diagnostic modality, go with simple spirometry.</p> <p>- USMLE cares about both outpatient management of asthma as well as acute attacks.</p> <p>- For outpatient management:</p> <ol style="list-style-type: none"> 1) First-line Tx is β2-agonist (albuterol) for acute attacks. 2) If the Q says the patient has weekly episodes, or they ask for what could decrease risk of future episodes if patient is already

	<p>on albuterol, the answer is inhaled corticosteroid (ICS; i.e., fluticasone).</p> <p>3) If the combo of albuterol + ICS is insufficient, the next step is increasing the dose of the ICS.</p> <p>4) If that doesn't work, adding a LABA (i.e., salmeterol) is the next step.</p> <p>5) If insufficient, agents such as mast cell stabilizers, leukotriene blockers, etc., can be tried. If patient has Hx of aspirin allergy, the latter in particular can be effective.</p> <p>6) Last resort for outpatient asthma is oral prednisone. It is most effective at decreasing recurrence of episodes, but we want to avoid it if at all possible because of the risk of Cushing syndrome and ↓ linear bone growth in Peds.</p> <ul style="list-style-type: none"> - Acute management of severe asthma attack (i.e., not outpatient) is nebulized albuterol, oxygen, and IV methylprednisolone. Inhaled corticosteroids have no role in acute asthma management. - NBME for 2CK wants you to know that any asthma patient who requires hospital management for an acute episode must automatically be given ICS (i.e., fluticasone) on discharge. In other words, if patient isn't currently on an ICS, it must be commenced at discharge. I'm explicit here because this particular NBME Q doesn't mention albuterol anywhere in the stem, but inhaled fluticasone is the answer. - Another 2CK NBME Q gives a patient who is currently not receiving any asthma medications but who gets 2+ episodes weekly → answer = "inhaled fluticasone + albuterol." Students think this is weird because they jump straight to dual management + are even audacious enough to put the ICS before albuterol in the wording of the answer, but it's what they want. Any patient with 2+ episodes per week needs ICS in addition to the albuterol and can be commenced right away on dual therapy.
Bronchiectasis	<ul style="list-style-type: none"> - Dilation of the airways (ectasia means dilation) that occurs due to "loss of musculature of the airways." - Transverse CT scan will show cystic dilation of the airways. <div data-bbox="743 1263 1222 1655" data-label="Image"> </div> <ul style="list-style-type: none"> - Most common cause worldwide is TB. Most common cause in western countries is CF. But on USMLE, it will usually be a smoker. Asthma does not cause bronchiectasis. - Presents almost always as "cups and cups of foul-smelling sputum." - "Foul-smelling" means anaerobes, such as <i>Bacteroides</i>. - One question on 2CK form gives bronchiectasis as the answer in a child who has right middle lobe syndrome, where they say there is scant white sputum (not cups and cups) and a thin, linear opacity visualized in the right middle lobe. If you think it's weird, complain to NBME not me. - Clubbing tends to be seen in these patients. It's not mandatory, but it's to my observation USMLE likes it for bronchiectasis.

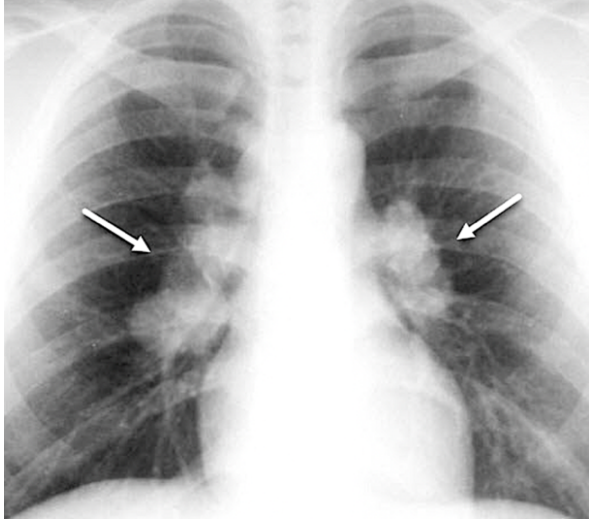
Atelectasis	<ul style="list-style-type: none"> - Confusing word that refers to “lung collapse,” or “collapse of alveoli.” - Highest yield point for USMLE is that it is the most common cause of fever within 24 hours of post-surgery. If this is the first time you’re reading this, that might sound weird, but this is pass-level and extremely important for 2CK. - There is one 2CK Q I’ve seen where they say a woman had a C-section two days ago and the answer was still atelectasis, so even though it’s most common <24 hours, just be aware one Q exists where, oh em gee, it’s 2 days later. - The mechanism is related to combo of pain meds + sedentation, where breathing becomes slower + shallower in hospital bed, leading to mild collapsing of some alveoli. This is why breathing exercises can be important post-surgery. - Will often present as bibasilar shadows or opacities. In other words, patient had surgery yesterday + now has fever + CXR shows mild opacity at the lung bases → answer = atelectasis. - NBME assesses obstructive (aka resorptive) atelectasis. This is when an area of lung distal to an obstruction from, e.g., a tumor, can cause alveoli to collapse. This then increases the chance for pneumonia distal to the obstruction. - 2CK IM form has “endobronchial obstruction” as answer for distal area of lung collapse (i.e., atelectasis) in patient with lung cancer; “vascular occlusion by tumor” is wrong answer (makes sense, as the tumor obstructs the respiratory tree, not blood vessel, in this case, but I’ve seen students accidentally choose the latter).
Obstructive sleep apnea (OSA)	<ul style="list-style-type: none"> - Can be obstructive (i.e., usually from obesity) or central (i.e., brain-related). What USMLE wants you to know: - These patients develop chronic respiratory acidosis – i.e., $\uparrow \text{CO}_2$, \uparrow bicarb, $\text{pH} \leftrightarrow \downarrow$. - Cor pulmonale can occur as a result of pulmonary hypertension from hypoxic vasoconstriction. JVD or peripheral edema will be seen with cor pulmonale. Descriptors such as RBBB, right-axis deviation on ECG, and wide splitting of S2 all mean RVH. If the patient merely has pulmonary hypertension but not yet cor pulmonale, the vignette can say loud P2 or tricuspid regurg (holosystolic murmur that \uparrow with inspiration). - Chronic fatigue and poor oxygenation can lead to dysthymia / depression. The answer on NBME is “mood disorder due to a medical condition.” - Polysomnography (sleep study) is what USMLE wants to diagnose.
Anaphylaxis	<ul style="list-style-type: none"> - Acute dyspnea and bilateral wheezes in patient who was gardening (stung by a bee), who ate a particular food (e.g., peanuts), or who was commenced on a recent drug (e.g., TMP/SMX). - Vignette often gives tachycardia and low BP. - Mechanism is IgE crosslinking on surface of mast cells and basophils that leads to degranulation and histamine + prostaglandin release. Eosinophils can be recruited in response. - USMLE wants: \downarrow vascular resistance, $\uparrow \text{CO}$, $\downarrow / \leftrightarrow \text{PCWP}$. - Tx = intramuscular epinephrine → the strong β_2-agonistic effect opens the airways; the strong α_1-agonistic effect constricts the arterioles and restores BP. - NBME for 2CK asks, “In addition to self-injectable epinephrine therapy, what is most appropriate therapy to \downarrow recurrences” → answer = venom immunotherapy (VIT). What this does is desensitizes the patient to the antigen by allowing him/her to develop neutralizing IgG antibodies against it.
Scombroid	<ul style="list-style-type: none"> - Often misdiagnosed as seafood allergy.

	<ul style="list-style-type: none"> - Bacteria in decaying meaty fish (e.g., mahimahi) can break down histidine in the fish into histamine, which causes an allergic-/asthma-like presentation. - Patients with history of asthma have greater risk of mortality.
Shellfish allergy	<ul style="list-style-type: none"> - Can cause allergic-/asthma-like presentation. - Occurs literally after eating shellfish (i.e., clams, mussels). - Don't confuse with scombroid. Students get trigger-happy when they learn weird conditions. If USMLE gives shellfish, the answer is shellfish allergy, not scombroid. The latter is from meaty fish and not an allergy.


HY Congenital lung diseases	
Cystic fibrosis	<ul style="list-style-type: none"> - Autosomal recessive; chromosome 7. - Mutations in <i>CFTR</i> gene, which codes for a chloride channel. - Most common mutation is $\Delta F508$, which is deletion of a phenylalanine. - USMLE wants "abnormal protein structure," or "abnormal protein folding," a common mechanistic answer for CF. - In the disease, the CFTR chloride channel, normally located at the cell surface, is instead sequestered at the RER. This is a HY point, where they want you to know patients with disease do <i>not</i> have the chloride channel on the cell membrane. - Disease results in impaired ability to secrete Cl^- into alveolar and pancreatic secretions. This causes greater (-) charge within the cell. Na^+ then moves through \uparrow ENaC into the cell to balance charge. Water follows Na^+, resulting in dried up alveolar and pancreatic secretions. These are known as inspissated secretions. Inspissation means desiccated (dried up) within a lumen. The inspissated alveolar secretions lead to mucous plugging, airway obstruction, and recurrent pneumonias. The inspissated pancreatic secretions lead to "exocrine pancreatic insufficiency" (HY phrase) and fat-soluble vitamin malabsorption. It is to my observation that vitamin E deficiency is the highest yield vitamin deficiency due to CF across NBME questions, which will present as neuropathy in a child who has CF. - Meconium ileus HY; refers to failure to pass stool in the first 24 hours after birth. - CF can sometimes cause nasal polyps. - USMLE doesn't obsess over pathogen causes for CF pneumonia, but classically <i>Pseudomonas</i> is a culprit. Prior to age 10, <i>S. aureus</i> exceeds <i>Pseudomonas</i> as most likely organism; after age 10, <i>Pseudomonas</i> eclipses <i>S. aureus</i>. The caveat is you have to use your head though: if they say 8-year-old with pneumonia due to gram-negative rods, you know that's <i>Pseudomonas</i>. Likewise, if they say a 17-year-old with pneumonia due to gram-positive cocci in clusters, you know that's <i>Staph aureus</i>. - Sweat glands reabsorb Cl^- rather than secrete it. This is impaired in CF, so we have \uparrow Cl^- in the sweat (i.e., >60 mEq/L). The sweat chloride test is more accurate for diagnosis than genotyping due to allelic heterogeneity of <i>CFTR</i> gene, where many different mutations cause the disease and can be difficult to detect with routine screening panels. - A transepithelial nasal voltage test can also be done, where there is \uparrow nasal potential difference. - Male patients can have congenital bilateral absence of vas deferens (CBAVD), leading to absent sperm in a sample. - Since this is an AR condition, there is a 2/3 chance a phenotypically normal sibling of a CF patient is a carrier. This applies to any AR disorder, but USMLE likes to use CF as the archetypal example. If this 2/3-point sounds confusing, I talk about this stuff in detail in my HY Genetics PDF.

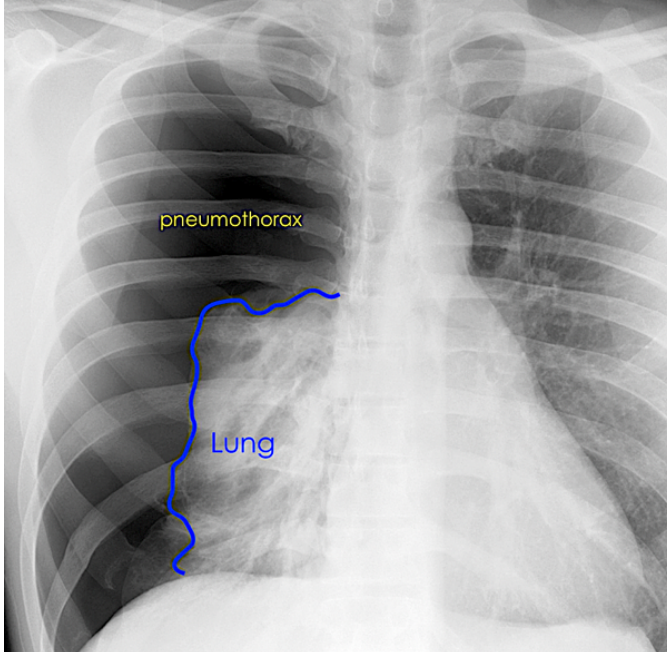
	<ul style="list-style-type: none"> - CF medications not HY for Step, but you could be aware that -caftor agents (e.g., ivacaftor, lumacaftor) facilitate with proper CFTR channel localization to the cell membrane + structural folding. - Dornase-alfa (correct, not alpha) is a nucleotidase that softens mucous. - Guaifenesin is also a mucous-softening agent.
Primary ciliary dyskinesia (Kartagener syndrome)	<ul style="list-style-type: none"> - Answer on USMLE for a question that sounds like CF but patient has situs inversus or dextrocardia – i.e., patient will have recurrent pneumonias and organs (or just heart) on opposite side of body. - Abnormality of cilia function due to defective dynein arm. This is a HY point, where sometimes the answer will just be “dynein.” - A cilium on cross-section has a 9x2 microtubule configuration. Dynein is a molecule that is necessary for cilia function.  <ul style="list-style-type: none"> - Patient will sperm in sample, but motility will be decreased. This is in contrast to CF, where sperm are absent due to CBAVD. - Women can get ectopic pregnancy due to abnormal Fallopian tube cilia. - This diagnosis sounds straightforward enough, but I’ve seen plenty of students miss these questions. For the situs inversus, they will describe this as cardiac sounds loudest on the right, or there being a large mass palpable beneath the left costal margin (liver on the opposite side).
Primary pulmonary hypertension (PPH)	<ul style="list-style-type: none"> - Answer on USMLE for a woman 20s-30s, non-smoker, who has increased pulmonary vascularity/markings and either a loud P2 or tricuspid regurg (as I talked about in cardio section, these are HY findings for pulmonary hypertension). - “Primary” means the pulmonary hypertension inherently <i>starts with</i> the lungs and is not due to a secondary (i.e., external) cause such as smoking, CF, systemic sclerosis, etc. - Due to mutations in BMPR2 gene. - Do not confuse this with cor pulmonale. Recall that the latter is right heart failure findings or RV structural changes due to a pulmonary cause. If the question gives evidence of RVH (i.e., RBBB, right-axis deviation on ECG, boot-shaped heart on CXR), or has overt right heart failure findings (i.e., JVD or peripheral edema), then we can say the patient now has cor pulmonale due to primary pulmonary hypertension. A loud P2 and tricuspid regurg, however, are HY findings for pulmonary hypertension that don’t necessarily mean cor pulmonale. - One of the highest yield points is that endothelin-1 is \uparrow in these patients. This is a vasoconstrictor that is \uparrow in pulmonary hypertension from any cause, but notably USMLE likes it for PPH. - Bosentan blocks endothelin-1 receptors and is HY Tx.

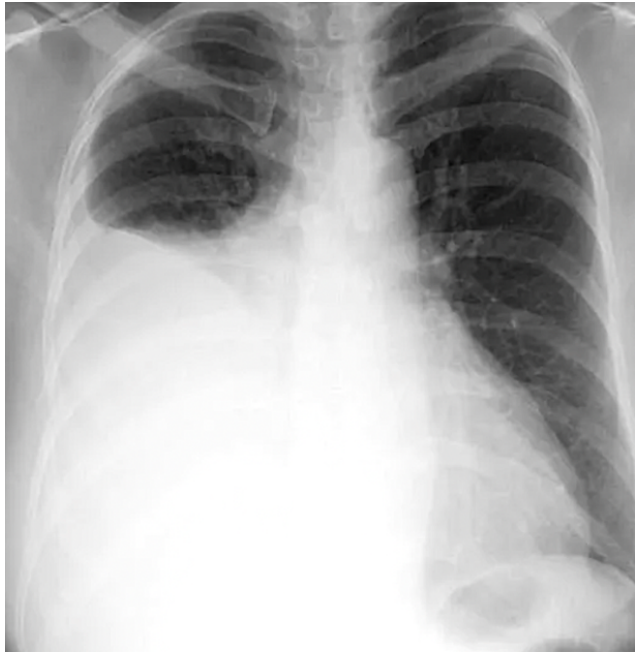
HY Autoimmune-related pulmonary conditions	
Systemic Sclerosis (aka scleroderma)	<ul style="list-style-type: none"> - Idiopathic autoimmune disease characterized by multi-organ system fibrosis and hardening of tissues (i.e., sclerosis). - Divided into limited and diffuse subtypes. - Limited scleroderma = CREST syndrome (Calcinosis, Raynaud's, Esophageal dysmotility, Sclerodactyly, Telangiectasias). - USMLE can describe Raynaud as color change of the fingers with cold weather. They describe sclerodactyly as tightening of the skin of the fingers. Esophageal dysmotility presents as GERD. I haven't seen NBMEs give a fuck about calcinosis, which is abnormal Ca^{2+} deposition in tissues. - Diffuse scleroderma = CREST syndrome + renal involvement (presenting as ultra-HY BP, e.g., 220/120, due to renal involvement causing a surge in RAAS. If patient doesn't have high BP, it's not diffuse type on USMLE. - Apart from just being able to diagnose these conditions, the highest yield point on USMLE is that both types cause pulmonary fibrosis, leading to pulmonary hypertension. - Pericardial fibrosis can also occur. - An offline NBME wants \downarrow LES sphincter tone and \downarrow esophageal peristalsis as an answer. - USMLE wants "dress warmly in cold weather" as an answer for how to \downarrow recurrence of Raynaud. Dihydropyridine CCBs can also be used (e.g., nifedipine), which \uparrow arteriolar + capillary diameter. - USMLE wants to know which drugs you avoid in patients with Raynaud \rightarrow answer = $\alpha 1$ agonists (e.g., phenylephrine, oxymetazoline), since these constrict arterioles/capillaries.
Sarcoidosis	<ul style="list-style-type: none"> - Idiopathic autoimmune disorder that is one of the highest yield conditions on USMLE. You must know this condition extremely well. - Characterized by non-caseating granulomas within lung tissue. These consist of activated macrophages called epithelioid macrophages, aka histiocytes. - These histiocytes in the lung secrete 1α-hydroxylase (normally produced in the PCT of the kidney in response to PTH), which will convert inactive 25-OH-D3 into active 1,25-(OH)$_2$-D3 (i.e., causing high vitamin D; aka hypervitaminosis D), which then goes to the small bowel and \uparrow absorption of calcium, causing hypercalcemia. - Even though 1,25-(OH)$_2$-D3 also \uparrow small bowel absorption of phosphate along with calcium, it's to my observation that phosphate can be <i>normal</i> in sarcoidosis NBME Qs, so do not be confused if you see phosphate in the normal range and only see hypercalcemia. - PTH is <i>suppressed</i> in sarcoidosis due to the high Ca^{2+} (exceedingly HY). - In other words, on USMLE you will select \uparrow 1,25-(OH)$_2$-D3 and \downarrow PTH. - Archetypal presentation is African-American woman 20s-30s with 6+ months of dry cough and red shins (erythema nodosum). Other findings like low-grade fever with flares can occasionally be seen. - Bihilar lymphadenopathy seen on CXR or CT. They can also describe this as CXR or CT "shows hilar nodularity."

	 <ul style="list-style-type: none"> - There is a 2CK Q that gives early-30s African-American woman with dry cough + they say CXR shows no abnormalities → answer = “activation of mast cells” (i.e., asthma is the answer); wrong answer is “non-caseating granulomatous inflammation.” So your HY point here is: if the vignette sounds like it could be sarcoidosis but they say CXR is normal or shows “mild hyperinflation” (also buzzy for asthma), choose asthma over sarcoidosis. - A 2CK IM CMS form gives a sarcoidosis vignette where they mention bihilar lymphadenopathy on a CT scan + high hepatic AST + ALP + weight loss; they don’t mention hypercalcemia. Unusual combo of findings, but the answer is inferable based on the CT. - Lupus pernio is an enlarged nose due to sarcoidosis (not SLE, despite the name). - USMLE wants steroids (i.e., oral prednisone) as treatment.
Rheumatoid lung	<ul style="list-style-type: none"> - Rheumatoid arthritis can cause a restrictive lung disease known as rheumatoid lung. - In addition, methotrexate, the first-line DMARD for RA, can cause pulmonary fibrosis. So patients with advanced RA can have pulmonary fibrosis from a combo of the two.

HY Pulmonary embolic conditions	
Pulmonary embolism	<ul style="list-style-type: none"> - DVT that has embolized up the venous circulation to the pulmonary arteries. - Presents as acute-onset shortness of breath and tachycardia in patient with one of the following risk factors: post-surgery (including C-section); sedation, e.g., due to trauma such as hip injury; OCP use; and thrombotic disorders (i.e., FVL, prothrombin mutation, MTHFR). - S1Q3T3 is most specific finding on ECG for PE that is nonexistent on USMLE and will get you questions wrong. What you want to remember is: sinus tachycardia (i.e., normal ECG but HR is simply high) is the most common ECG finding for PE. - First step in management (2CK) is heparin. - After heparin, do a spiral CT of the chest to diagnose. - If the patient is already on warfarin and gets a PE, the first answer they want is CT to diagnose, followed by IVC filter. Do not choose IVC filter prior to confirming the PE with a CT. - One 2CK NBME Q has tPA as the answer for PE in patient who has obstructive shock (i.e., low BP due to PE). - V/Q scan is done instead of CT first-line in pregnancy. - One 2CK Q gives V/Q that is performed and shows “multiple sub-segmental perfusion defects” → answer = recurrent pulmonary emboli. - Most common cause of death from PE is ventricular fibrillation → acute right heart strain from a saddle embolus precipitates the Vfib.

	<ul style="list-style-type: none"> - The acid-base arrows USMLE wants for PE are: \downarrow CO₂, \uparrow pH, \leftrightarrow bicarb. In other words, we have an acute respiratory alkalosis from high RR. Bicarb is unchanged because the kidney requires minimum 12 hours to accomplish this. These arrows are the same as acute asthma attack. - One 2CK Q gives lab values in PE of \downarrow CO₂ and \downarrow pH. What this means is: patient has lactic acidosis (hence \downarrow bicarb) due to ischemia from poor perfusion. It's HY for USMLE that you know any cause of shock, whether that be septic, hypovolemic, cardiogenic (or even obstructive from PE), can cause lactic acidosis and low bicarb. Don't be confused by this. - PE is textbook example of dead space (as discussed earlier).
Amniotic fluid embolism	<ul style="list-style-type: none"> - The answer on USMLE if they say 30 seconds to 2 minutes after delivery of the placenta, the patient gets shortness of breath and tachycardia \rightarrow sounds like PE, but answer is amniotic fluid embolism to the lungs. In contrast, if they say a woman had a C-section 2 days ago + now gets up in hospital to use bathroom + now has acute-onset SoB and tachycardia \rightarrow answer = PE, not amniotic fluid embolism. - Can cause disseminated intravascular coagulation (DIC). It's one of the weird causes for USMLE. They can say the patient has bleeding from IV sites / catheter lines following delivery of the placenta.
Fat embolism	<ul style="list-style-type: none"> - The answer on USMLE if they say long-bone fracture (i.e., usually femur) in patient who now develops shortness of breath + petechiae on the shoulders/chest. - The patient will also have thrombocytopenia, but only about half of vignettes mention this. - The petechiae on the shoulders/chest are not due to the \downarrow platelets, since conditions like ITP, for instance, don't present with this finding. Literature suggests it might be related to microvascular plugging by fat in the dermis. - Question can mention pulmonary biopsy stained with Oil Red O or Sudan black (stains for fat).
Air embolism	<ul style="list-style-type: none"> - The answer on USMLE if they say patient has sudden death following insertion of a central venous line \rightarrow air goes to the lungs + kills patient.
Cholesterol embolism	<ul style="list-style-type: none"> - Will present as two ways on USMLE: 1) violaceous lesions on the feet in someone who just had a AAA repair \rightarrow cholesterol plaque launches off to feet + they show you image like this one below:  <p>The second way (2CK NBME 10) has cholesterol emboli Q where they don't show an image but describe the violaceous foot lesions in someone with mere Hx of AAA (rather than undergoing repair). They say "Maltese crosses are seen." Obscure, but apparently refers to birefringence of cholesterol esters that can be visualized under polarized light.</p>

HY Trauma and pleural space conditions	
Pulmonary contusion	<ul style="list-style-type: none"> - Difficult diagnosis on 2CK forms. - Diagnosis of exclusion, meaning all of these 2CK Qs require eliminating the other answer choices to get there. - The Q will say patient was in an accident + now has some form of difficulty breathing and patchy infiltrates in one or more areas of lung. They may or may not mention rib fractures just above the areas of infiltrates. Sounds vague as I said, but that's what USMLE will say. - Textbook descriptors such as "white-out of the lung" are nonsense. I don't think I've ever seen this on NBME material. - Contused (bruised) lung is known to be fluid-sensitive, where the Q can say patient was given IV saline and now has worsening of O2 sats. This is classic, but I've also seen this in myocardial contusion questions, making the Dx difficult as I said. But you'll be able to eliminate myocardial contusion if they don't mention severe bruising or pain over the sternum or post-MVA arrhythmia (e.g., premature atrial contractions).
Flail chest	<ul style="list-style-type: none"> - The answer on 2CK forms if they say a patient has paradoxical breathing (i.e., the chest wall moves outward with expiration and inward with inspiration).
Ruptured bronchus	<ul style="list-style-type: none"> - The answer on 2CK forms if they say there's a "persistent air leak despite placement of a chest tube." This will be in a trauma patient.
Diaphragmatic rupture	<ul style="list-style-type: none"> - The answer on 2CK forms for an MVA followed by CXR showing "obscured left hemidiaphragm and the NG tube present in the lower left side of the chest." - Don't confuse with ruptured bronchus above, or with esophageal rupture, which will tell you water-soluble contrast swallow is visualized in the mediastinum.
Pneumothorax	<ul style="list-style-type: none"> - Air in the pleural space. The terms almost always refers to a "spontaneous pneumothorax," which will be acute-onset sharp chest pain in a tall, lanky patient in teens or 20s due to "ruptured subapical bleb."  <ul style="list-style-type: none"> - Pneumothorax + low BP = tension pneumothorax. - Mechanism for tension pneumothorax is compression of the vena cava leading to ↓ venous return → can cause JVD. - Simple/spontaneous pneumothoraces cause ipsilateral tracheal shift. - Tension pneumothoraces cause contralateral tracheal shift. - Tension pneumothorax need not be due to overt trauma. It will literally just be pneumothorax + low BP 9/10 times on USMLE. I've seen only one Q on a 2CK

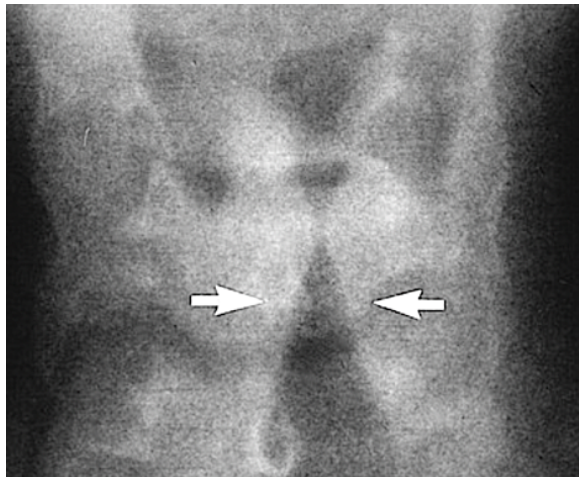
	<p>form where BP is lower end of normal, but the patient is tachy around 120 bpm (implying barely holding BP in normal range).</p> <ul style="list-style-type: none"> - Patient will have hyper-resonance to percussion, ↓ breath sounds, and ↓ tactile fremitus. Breath sounds are ↓ because the air in the pleural space masks the sounds of underlying air flow in the alveoli. Tactile fremitus is ↓ because the vibration of air in the alveoli is masked by the overlying air. - Treatment for pneumothorax is “needle decompression followed by chest tube.” That phrase is HY. - One 2CK Q just has “tube thoracostomy” as the answer without needle decompression being listed. So if they don’t list the needle, don’t be confused, and just choose the chest tube. Thoracostomy means making a hole in the thorax. - Pleurodesis I’ve never seen as correct answer on NBME material but can be listed as distractor → means putting talc into pleural space to obliterate it in patients who have recurrent pneumothoraces. - Should be noted that very small pneumothoraces in stable patients with minimal symptoms can be observed. There is one Q on a 2CK NBME form where the answer is observe. But the vignette goes out of its way to emphasize how unremarkable the patient’s presentation is. - There is a 2CK Q where pneumothorax is caused by barotrauma from ascending too quickly from underwater. This is different from Caisson disease (“the bends”), where nitrogen bubbles form in the blood. Pulmonary barotrauma from quick ascent, resulting in pneumothorax, can occur if some of the alveoli expand too quickly.
Pleural effusion	<ul style="list-style-type: none"> - Fluid in the pleural space; often refers to “hydrothorax,” which means transudate or exudate of plasma-like fluid.  <ul style="list-style-type: none"> - USMLE wants: dullness to percussion, ↓ breath sounds, and ↓ tactile fremitus. Similar to pneumothorax, the latter two are ↓ because the fluid in the overlying pleural space masks air movement in the alveoli. - Many causes of pleural effusion on USMLE. I’ve observed left heart failure as a notable cause (i.e., patient will have pulmonary edema +/- pleural effusion). NBME can also give you pleural effusion with pneumonias, tuberculosis, and aortic dissection. - Meigs syndrome = triad of ovarian fibroma, ascites, right-sided pleural effusion.

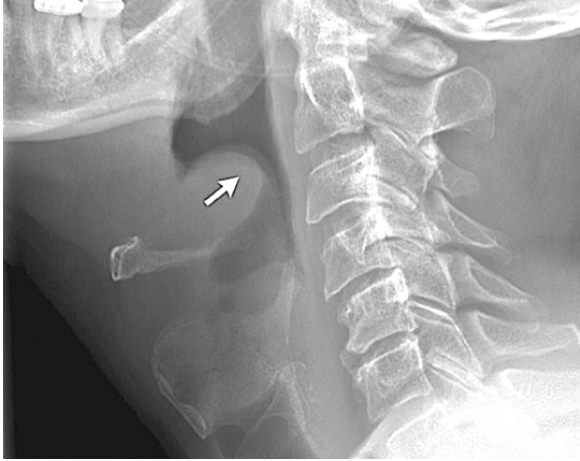
	<ul style="list-style-type: none"> - USMLE wants you to know transudative versus exudative pleural effusions → transudates are more water-like, with fewer solutes; exudates contain more solutes. As per Light's criteria (HY for both Steps 1 and 2CK), an exudate will have: <ul style="list-style-type: none"> - Pleural fluid protein : serum protein ratio >0.5. - Pleural fluid LDH : serum LDH ratio > 0.6. - Pleural fluid LDH >2/3 upper limit of normal of serum LDH. - In other words, transudate contains less protein and LDH as the two main distinctions. - Transudates contain fewer WBCs than exudates, but I routinely see 500 WBCs/μL in transudate Q on NBME. - Highest yield cause of transudate on USMLE is left heart failure, as discussed in the Cardio PDF. - ARDS, pulmonary emboli, and infections can cause exudative pleural effusions (due to inflammation). - Progression to empyema HY (see below).
Empyema	<ul style="list-style-type: none"> - Two ways empyema presents on NBME: - 4 out of 5 questions, it will present as a sequence of pneumonia → parapneumonic effusions (i.e., exudative pleural effusions that occur due to pneumonia) → empyema. In other words, if a patient has a pneumonia that then leads to an exudative pleural effusion, we simply call that a parapneumonic effusion. This effusion can become progressively worse and purulent, to the point that the pH of the pleural fluid falls below ~7.1ish. We now call it empyema, which is frank pus in the pleural space. Low pH of the pleural fluid to < ~7.1 is very HY on 2CK forms. I've seen Qs where they say 7.12, 7.11, and 6.99, and they want empyema. - 1 out of 5 Qs will not mention anything about Hx of pneumonia. They will give patient who has persistent fever + recurrent pleural effusions in someone who has cirrhosis (i.e., ↓ oncotic pressure → transudative pleural effusions). Then the answer is just empyema. - NBME wants tube thoracostomy to drain the purulence.
Chylothorax	<ul style="list-style-type: none"> - Chyle (lymph fluid) in the pleural space. - The answer when they tell you a patient has milky or white-cloudy fluid in the pleural space where the pH is significantly above 7.1. - For instance, they might give you 15-line paragraph where they say milky fluid + tons of lab values, but you notice the pH of the pleural fluid is 7.40. This means it's chylothorax and empyema is wrong. - Can be caused iatrogenically by insertion of central line via the left internal jugular vein, or by cancers, e.g., lymphoma.
Hemothorax	<ul style="list-style-type: none"> - Blood in the pleural space. - Apart from massive trauma, the way this shows up on USMLE is as malignant pleural effusion. - They'll give you massive paragraph with tons of info + tell you patient has history of breast or lung cancer + has dullness to percussion → answer = malignant pleural effusion. - Patient can have hypotension and muffled heart sounds, similar to cardiac tamponade, but rather than JVD (to complete Beck triad), can have flattened neck veins (due to loss blood from the circulation).

HY Alveolar fluid conditions	
Pulmonary edema	<ul style="list-style-type: none"> - Due to left heart failure on USMLE. - There is such thing as “non-cardiac pulmonary edema” (i.e., ARDS, TRALI [discussed below in this table]), but for USMLE purposes, if you see “pulmonary edema” as an isolated phrase, it refers to transudation of fluid into the alveolar spaces due to \uparrow pulmonary capillary hydrostatic pressure from left heart pathology. - PCWP and LAP are both elevated. - USMLE can give you vignette of, e.g., MI with dyspnea, and they ask for the mechanism of the dyspnea in the patient \rightarrow answer = “increased alveolar-arteriolar oxygen gradient” – i.e., the patient can breathe just fine so alveolar O₂ is normal, but fluid impairs the gas exchange, so we have low arterial/arteriolar oxygen. - “Cephalization of pulmonary vessels” is buzzy and synonymous with pulmonary edema on USMLE. Shows up in some NBME vignettes.
Acute respiratory distress syndrome (ARDS)	<ul style="list-style-type: none"> - The answer on USMLE for bilateral exudative chest infiltrates and \downarrow O₂ sats in patient following: pancreatitis; aspiration of vomitus; near-drowning episodes (aspiration of fresh/sea water); improper insertion of NG tube into the lungs with feeding initiated; toxic shock syndrome; or general trauma / sepsis. - 2CK NBME Q gives vignette of toxic shock syndrome and then asks most likely cause of death in this patient \rightarrow answer = ARDS. - Pulmonary decompensation associated with pancreatitis is very buzzy. - Another 2CK Q gives patient who is brought to hospital following near-drowning episode + they ask what the patient needs to be monitored for \rightarrow answer = ARDS. - ARDS is technically defined as a PaO₂/FiO₂ <300, but USMLE doesn’t give a fuck. I’ve never once seen them apply this ratio or care. - I emphasize up above the bilateral nature of ARDS because many Qs give ARDS as DDx for unilateral conditions and it’s wrong. - In theory, patient can be ventilated as follows: prone positioning (patient on stomach) + low-tidal volume setting + permissive hypercapnia. IIRC this is asked once on a 2CK form. - An offline NBME Q wants “increased surfactant protein D” as the answer in a patient who is recovering from ARDS. Apparently surfactant protein D is a marker of lung injury and is \uparrow in patients with ARDS (or who are recovering from it). Call it weird all you want but it’s on the NBME.
Transfusion-associated lung injury (TRALI)	<ul style="list-style-type: none"> - The answer on USMLE if a patient has an ARDS-like presentation with bilateral crackles and low O₂ sats <6 hours following a transfusion. - Mechanism is abnormal priming of neutrophils in the lung that react to cytokines within transfused blood products. - This is technically a type of non-cardiogenic pulmonary edema.
Transfusion-associated circulatory overload (TACO)	<ul style="list-style-type: none"> - Aka transfusion-induced hypervolemia. - Differs from TRALI in that this is a type of cardiogenic pulmonary edema (i.e., the left heart can’t handle the \uparrow hydrostatic pressure from \uparrow volume, so transudation into the alveoli occurs). - Annoying diagnosis but presents two ways: <ol style="list-style-type: none"> 1) If a patient <i>with Hx of heart failure or MI</i> develops respiratory distress following transfusion of repeated blood products. <ul style="list-style-type: none"> - A 2CK NBME Q gives a 72-yr-old with Hx of MI ten years ago who gets shortness of breath and bilateral crackles 30 minutes after transfusion with crystalloid solution and 4 packs of RBCs (they don’t specify the volume of crystalloid in the Q). 2) They don’t mention Hx of cardiovascular disease + the vignette will sound exactly like TRALI > 6 hours following a transfusion.

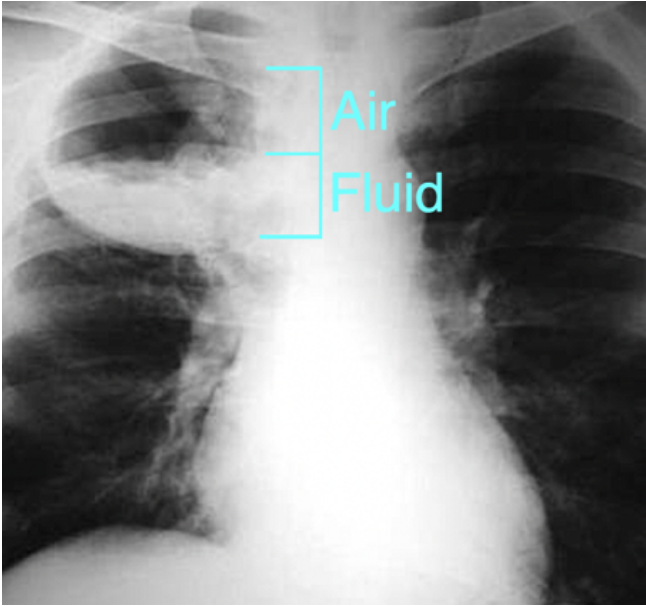
	<p>- 2CK form gives an elderly dude who received only 3 packs of RBCs + he develops bilateral crackles and low O2 sats, but they say this occurs 12 hours after admission (not <6 hours as with TRALI), where the answer is "X-ray of the chest" as the next best step in diagnosis. The Q doesn't rely on you discerning TACO vs TRALI to get it right, but the explanation says it's TACO.</p> <p>In summary, if ARDS-like picture after transfusion:</p> <p>If <6 hours → TRALI. If >6 hours → TACO. If heart disease → TACO regardless of time frame.</p>
--	--

HY Infection-related stuff	
Pneumonia	<ul style="list-style-type: none"> - Lobar pneumonia = <i>Strep pneumoniae</i> on USMLE (right lower lobe consolidation with dullness to percussion). - Bilateral interstitial pneumonia (aka atypical pneumonia) in immunocompetent patients = <i>Mycoplasma</i> on USMLE. - Lobar pneumonia where they say "interstitial markings" and <i>Strep pneumo</i> isn't listed → answer = <i>Mycoplasma</i> (the word "interstitial" wins over location). - Bilateral interstitial / "ground-glass" pneumonia in AIDS patient → <i>Pneumocystis jirovecii</i> pneumonia (PJP). - Lobar pneumonia in AIDS patient → <i>Strep pneumo</i>, not PJP. - Bacterial pneumonia specifically post-influenza infection → <i>S. aureus</i>. - Bilateral pneumonia + low Hb or (+) Coombs test → <i>Mycoplasma</i> → can cause cold agglutinins, which means IgM against RBCs → hemolysis). - Pneumonia + hyponatremia and/or diarrhea → <i>Legionella</i>. - Pneumonia + business conference or residential home (implies air conditioners) → <i>Legionella</i>. - Pneumonia in 3-wk-old neonate who had conjunctivitis 1-2 weeks ago → <i>Chlamydia trachomatis</i> (the STI; drains through nasolacrimal duct to lungs). - Pneumonia in newborn first few days of life → Group B Strep (<i>Strep agalactiae</i>), which is gram (+) cocci. If they say gram (+) rods, that's instead <i>Listeria</i>. If they say gram (-) rods, that's <i>E. coli</i>. - Pneumonia + rabbits → <i>Francisella</i>. - Pneumonia + bird keeper → <i>Chlamydia psittaci</i>. - Pneumonia + southwest US and/or earthquake dust → <i>Coccidioides</i>. - Patients who have lung cancer are prone to obstructive pneumonias (on 2CK form). - Pneumonia in CF → <i>Pseudomonas</i> or <i>S. aureus</i>. - Pneumonia in patient with central venous catheter + right upper lobe lesion → answer = <i>Staph epidermidis</i> (on NBME). Catheter = biofilms. - USMLE wants for pneumonia: adventitious/bronchial (i.e., abnormal) breath sounds + ↑ tactile fremitus (air vibrates due to movement through infective consolidation within alveoli). - Community-acquired pneumonia (CAP) empiric Tx = azithromycin on 2CK (on NBME). This covers the atypicals (<i>Mycoplasma</i>, <i>Legionella</i>, <i>Chlamydia</i>) as well as <i>S. pneumo</i>. - If patient has been on antibiotics in the past 3 months or has severe lung disease, levofloxacin (respiratory fluoroquinolone) can be given first-line. - CAP that results in sepsis or septic shock → give ceftriaxone (if listed, choose cefotaxime for peds).

	<ul style="list-style-type: none"> - Nosocomial pneumonia (i.e., hospital- or ventilator-acquired) requires coverage for MRSA and <i>Pseudomonas</i>. USMLE wants vancomycin PLUS either ceftazidime (a 3rd-gen cephalosporin) or cefepime (a 4th-gen). - For fungal pneumonia, Tx = fluconazole. - For fungal pneumonia + fungemia (high fever, chills) → Amphotericin B. - NBME for 2CK wants you to know sputum culture, followed by blood cultures are done in all patients with pneumonia who are septic. What they do in this patient is give you patient who has sputum culture performed, then they ask what should be done next for diagnosis? → answer = blood culture. - If you get <i>Pneumocystis</i> pneumonia, jump straight to bronchoalveolar lavage as the answer. - If you get a patient who has CXR or CT showing cavitory lesions in the lungs filled with a mass (likely <i>Aspergillus</i> fungus ball), they want “open lung biopsy” as the most confirmatory test. - When a pneumonia fully resolves and USMLE asks why the CXR is normal after the fact, the answer is “maintenance of integrity of basement membranes,” as mentioned earlier. - 2CK wants you to know that pneumonias can occur in patients distal to areas of lung obstructed by tumors; the answer will be “endobronchial obstruction” as the reason the patient has distal pneumonia (same answer for why there can be distal atelectasis). - NBME wants you to know rituximab (monoclonal antibody against CD20 on B cells) increases the risk of bacterial pneumonia. This makes sense, since B cells are required for antibody production as part of humoral immunity against bacteria.
Bronchiolitis	<ul style="list-style-type: none"> - Answer on USMLE for a kid <18 months old who has low-grade fever and bilateral wheezes. - Caused by respiratory syncytial virus (RSV). - Tx is supportive care on USMLE. Don’t choose answers like ribavirin or palivizumab.
Laryngotracheal bronchitis (aka croup)	<ul style="list-style-type: none"> - Caused by paramyxovirus (aka parainfluenza virus). - Presents as hoarse, barking, or seal-like cough in school-age kid. The Q can say the cough gets better when his dad brings him out into the cold air. - Neck x-ray shows “steeple sign,” which is sub-glottic narrowing.  <ul style="list-style-type: none"> - Sometimes the Q can give you easy vignette of croup, but then the answer is just “larynx” (literally inflammation of the larynx, trachea, and the bronchi). “Sub-glottic” means below the area of the vocal cords. The larynx is the area encompassing the vocal cords. - Tx is supportive. If they force you to choose an actual Tx however, nebulized racemic epinephrine is the answer.

Epiglottitis	<ul style="list-style-type: none"> - Caused by <i>Haemophilus influenzae type B</i>. - Seen in unvaccinated and immigrants (can be unvaccinated), as well as patients with asplenia or sickle cell (auto-splenectomy). - Can also cause meningitis. - X-ray of neck shows "thumbprint sign."  <ul style="list-style-type: none"> - Presents as child who has fever + difficulty breathing. They can say the kid is drooling and/or in tripod positioning (facilitates use of accessory muscles). - USMLE wants intubation as answer. Epiglottitis is a medical emergency that can lead to sudden occlusion of the airway. - Tx = 3rd-gen cephalosporin (cefotaxime in peds, or ceftriaxone); give rifampin to close contacts.
Bacterial tracheitis	<ul style="list-style-type: none"> - Diagnosis of exclusion on USMLE (i.e., you eliminate to get there). - Classically caused by <i>S. aureus</i> following a viral URTI. - Shows up on 2CK form as patient with recent viral URTI who now has stridor (suggesting upper airway narrowing) + no drooling (suggests against epiglottitis) + can fully open the mouth without difficulty + does not improve with racemic epinephrine (suggests against croup). - Being able to open the mouth without difficulty is important because this contrasts with peritonsillar abscess, where the patient has difficulty fully opening the mouth.
Pertussis	<ul style="list-style-type: none"> - Classic whooping cough presents as succession of many coughs followed by an inspiratory stridor. - What you need to know for USMLE is that this can absolutely present in an adult and that they can be vague about it, just describing it as a regular cough. The way you'll know it's pertussis, however, is they will say there's either hypoglycemia or post-tussive emesis, which means vomiting after coughing episodes. - Pertussis can cause super-high WBC counts in the 30-50,000-range, where there are >80% lymphocytes. <i>This makes it resemble ALL</i>. So you should know for Peds that ALL-like laboratory findings + cough = pertussis. - Q will ask number-one way to prevent → answer = vaccination (not hard, but they ask it). Pertussis is part of TDaP. The pertussis component is killed-acellular; the tetanus and diphtheria are toxoid. - Erythromycin can be given to patients with active cough; USMLE doesn't give a fuck about pertussis stages. - Close contacts should also receive erythromycin.
Pleurodynia	<ul style="list-style-type: none"> - As mentioned in the Cardio section, this is an MSK condition I've seen asked twice on NBME that has nothing to do with the lungs, despite the name. - This is viral infection (Coxsackie B) causing sharp lateral chest pain due to intercostal muscle spasm.

	<ul style="list-style-type: none"> - Creatine kinase can be elevated in stem due to ↑ tone of muscle.
Tuberculosis	<ul style="list-style-type: none"> - <i>Mycobacterium tuberculosis</i> has unique cell wall composed of mycolic acid that is difficult to gram stain. Requires acid-fast stain. - Produces cord factor (asked on NBME) as a virulence factor. - Can present similar to lung cancer, where patient can have B symptoms (i.e., fever, night sweats, weight loss) and hemoptysis. - Living in a homeless shelter or immigrant status from endemic area is buzzy. I've seen rural India and Albania as two locations in NBME Qs. - Can cause cavitations and calcification in the lung grossly; on histo, causes caseating granulomatous inflammation. - Ghon foci/complexes are textbook descriptors for TB lesions but not assessed eponymously on USMLE. - Can cause constrictive pericarditis (can also calcify). - Disseminated TB (miliary TB) can affect multiple organ systems, leading to psoas abscess, Pott disease (TB infection of the vertebrae), adrenal insufficiency, meningitis, osteomyelitis, and arthritis. - First step in diagnosis is PPD test (type IV hypersensitivity). - If PPD test is (+), the next best step is CXR. - If PPD is (+) but CXR (-), next best step is "treat for latent TB," or "give TB prophylaxis." This is isoniazid (INH) for 9 months + vitamin B6 (since INH can cause B6 deficiency). It is exceedingly HY you know that neuropathy in a patient being treated for TB has B6 deficiency. - If PPD and CXR are both (+), the next best step is "treat for active TB," which is RIPE for 2 months + RI for 4 more months (6 months total). RIPE = rifampin, isoniazid, pyrazinamide, ethambutol. - BCG vaccine is live-attenuated. USMLE wants you to know Hx of BCG vaccine does not change management based on PPD guidelines. - If USMLE asks you how long after TB exposure will someone's sputum cultures be positive, the answer is 2-5 weeks. - Interferon-gamma release assay (Quantiferon Gold) can be used in patients who have Hx of BCG to ↓ false (+)s, but USMLE doesn't assess it. The reason I mention it is because they want you to know <i>interferon-γ</i> is required for stimulation of alveolar macrophages to control TB. - Patients who have IFN-γ deficiency or IL-12 receptor deficiency (IL-12 normally ↑ IFN-γ) have ↑ susceptibility to TB infections. If this immuno stuff sounds confusing, I talk about this in detail in my HY Immuno PDF. - TNF-α is also required to suppress TB. Therefore drugs such as infliximab, adalimumab, and etanercept ↑ risk of TB, which is why they should be avoided in silicosis patients, as mentioned earlier. - What is considered a positive PPD test differs depending on risk factors: <ul style="list-style-type: none"> - >5mm (+): Hx of close contact to someone with active TB; immunocompromised patient (AIDS, organ transplant recipient receiving immunosuppressants, chronic corticosteroid user); calcification on CXR. - >10mm (+): Health care worker or prisoner/prison worker; immigrant from endemic area; TB laboratory personnel, children <4. - >15mm (+): everyone else. - If a PPD test is (+), never repeat it. If it is negative, it must be repeated in 1-2 weeks (i.e., sometimes false-negatives).
Hot tub lung	<ul style="list-style-type: none"> - Answer on a 2CK form for a guy who moves into a new apartment building with a hot tub and gets bilateral chest infection → inhalation of fumes with <i>Mycobacterium avium complex</i> (MAC).

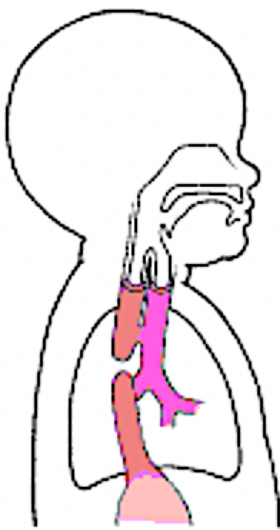
Pulmonary abscess	<ul style="list-style-type: none"> - Exceedingly HY on USMLE. - USMLE wants “aspiration of oropharyngeal normal flora,” or “aspiration of oropharyngeal anaerobes” as the cause. - Q will give aspiration risk factor, such as alcoholism, dementia (can cause loss of gag reflex), Hx of stroke (leading to dysphagia), or epilepsy. - Q can also mention broken or missing teeth (hypodontia) as risk factor. - Often described on NBME as pulmonary lesion with an air-fluid level. This is buzzy, but not a mandatory descriptor. This refers to the top half of the circle being air, and the bottom being pus, the latter settling due to gravity.  <ul style="list-style-type: none"> - The stem can say the patient has “foul-smelling sputum.” This descriptor is exceedingly HY and is synonymous with anaerobes on USMLE. - Oropharyngeal normal flora = <i>Bacteroides</i> (strictly anaerobic gram-negative rods); as well as <i>Peptostreptococcus</i> and <i>Mobiluncus</i>. The latter two are not HY, but <i>Bacteroides</i> is. I mention all three, however, because the Q can say sputum sample shows “gram-negative rods, gram-positive cocci, and gram-positive rods,” which refers to all three. But the bigger picture concept is, this = mixed normal flora. - Tx = clindamycin. USMLE loves this. - If Q tells you patient was treated for pulmonary abscess + a year later there’s still a lesion seen on CXR → answer = “failure of maintenance of basement membranes.”
Acute bronchopulmonary aspergillosis (ABPA)	<ul style="list-style-type: none"> - Presents as asthma-like presentation in patient with ↑ sensitivity to aspergillus skin antigen.
Hypersensitivity pneumonitis	<ul style="list-style-type: none"> - Answer on USMLE for bilateral lung condition + fever in farmer who has exposure to hay (on new NBME). - They will tell you the fever self-resolves after 2 days and he now is afebrile. - Byssinosis (pneumoconiosis from hemp) is wrong answer, since this won’t present with fever + classically presents in textile workers.
Cryptogenic organizing pneumonia (COP)	<ul style="list-style-type: none"> - Idiopathic restrictive lung disease where patient has pneumonia-like presentation that fails to improve with antibiotics. Not actual pneumonia. - Formerly known as bronchiolitis obliterans organizing pneumonia (BOOP). - Nonexistent yieldness on USMLE, but I mention it because you will sometimes see this as a <i>wrong</i> answer choice, particularly on hard 2CK Qs, and I’ve seen enough students erroneously pick it.
Otitis media (OM)	<ul style="list-style-type: none"> - Infection of portion of ear just deep to tympanic membrane. - Most commonly <i>Strep pneumo</i>.

	<ul style="list-style-type: none"> - Will present as red, immobile tympanic membrane. Immobility of the tympanic membrane is highly sensitive for OM, meaning that if the Q says mobility is normal, we can rule out. - "Ear tugging" can be a sign in children of either otitis media or externa. - Tx is amoxicillin or penicillin. - Augmentin (amoxicillin/clavulanate) is classically given for <i>recurrent</i> OM. So if you are forced to choose between amoxicillin/penicillin alone or Augmentin, go with the former. - For 2CK Peds, a tympanostomy tube (aka grommet) is used if the kid has >3 OM occurrences in 6 months, or >4 in a year.
Serous otitis media	<ul style="list-style-type: none"> - Aka otitis media with effusion. - Presents as fluid behind the tympanic membrane in a kid weeks after resolution of 1 or 2 otitis media infections. - Almost always benign and self-resolves in 4-8 weeks. Answer is observation.
Tympanic membrane perforation	<ul style="list-style-type: none"> - "Tympanic membrane perforation" is the answer on new 2CK NBME for 2-year-old who had 3-day Hx of viral infection followed by awakening with severe ear pain + has dried blood on ear lobe and pillow + otoscopy cannot visualize tympanic membrane because of seropurulent fluid draining from the ear canal. - Can occur due to otitis media, although vignette on NBME doesn't sound like classic OM and is as described above.
Mastoiditis	<ul style="list-style-type: none"> - Inflammation of mastoid bone caused by untreated otitis media. - The mastoid process is the posterior part of the temporal bone that is felt just behind the ear. - Can present as a painful ear pinna that is displaced (e.g., upward and outward). - Diagnosis is made by CT or MRI. X-ray is wrong answer. - 2CK IM Q gives a 2-year-old with mastoiditis where the answer is "CT of the temporal bone." Sounds wrong, since this is ↑ radiation for a kid, but it's what they want.
Myringitis	<ul style="list-style-type: none"> - Isolated inflammation of the tympanic membrane. - Can be bullous (i.e., bullous myringitis). - Caused by <i>Strep pneumo</i> or <i>Mycoplasma</i>.
Otitis externa (OE)	<ul style="list-style-type: none"> - Infection of ear superficial to tympanic membrane. - Classically caused by <i>Pseudomonas</i>. - Increased risk in swimmers and diabetics. - An NBME form has "necrotizing otitis externa" as answer for black skin within the ear canal in a patient. This is aka "malignant otitis externa." - USMLE wants "acetic acid-alcohol drops" as prophylaxis in college student who does crew + continues to have water exposure. - Tx (not prophylaxis) = "topical ciprofloxacin-hydrocortisone" drops.
Sinusitis	<ul style="list-style-type: none"> - The answer if they tell you a school-age kid has a lingering fever after an upper respiratory tract infection (URTI) for 10-14+ days. - Whenever a URTI lingers for more than ~10ish days, you want to think about sinusitis as a differential. - A 2CK vignette gives nocturnal cough (reflects aspiration; in this case, from the sinuses) and grey membranes in the oropharynx. - The grey oropharyngeal membranes detail sounds weird, since that is normally buzzy for <i>Diphtheria</i>, but it shows up on an NBME Q where the answer is sinusitis and <i>Diphtheria</i> isn't listed. - IgA deficiency Qs, which presents as recurrent sinopulmonary infections, can say patient has Hx of pneumonias + presents today with sore left cheek → reflects sinusitis. - For 2CK, CT scan is done if chronic sinusitis >12 weeks. After CT is performed for chronic sinusitis, nasal endoscopy can be performed.

	<ul style="list-style-type: none"> - Tx is amoxicillin/clavulanate (Augmentin). This is in contrast to OM and <i>Strep</i> pharyngitis, which are treated with just amoxicillin or penicillin alone, without the clavulanate (unless recurrent).
Influenza	<ul style="list-style-type: none"> - Causes respiratory distress, fever, and myalgias (muscle pain). For USMLE purposes, the myalgias are exceedingly HY as a vignette finding that usually suggests the flu over other diagnoses. - Has 8 segments, two of which are hemagglutinin and neuraminidase. - Hemagglutinin mediates viral attachment to the cell by enabling its binding at sialic acid receptors. - If a question asks about the molecule most flu vaccines are targeted against, the answer is hemagglutinin. - Neuraminidase allows for newly synthesized viral particles to leave the host cell. This enzyme cleaves sialic acid residues, which normally bind the new viral particles within the cell. Once these residues are cleaved, the viral particles can leave the cell. - Drugs such as oseltamivir and zanamivir are sialic acid analogues that function as neuraminidase competitive inhibitors. In other words, they prevent the virus from leaving the cell. If the USMLE asks which drug prevents viral spread within a community, or they tell you a drug is given and now host cells are "packed with virions" (because they can't leave the cell), the answer is one of the -mivirs. - Antigenic drift is point mutations in hemagglutinin and/or neuraminidase, where the virus has changed slightly. It leads to seasonal epidemics. Antigenic shift is due to two influenza viruses entering a cell, one of human origin, the other of animal origin (such as bird or swine), where they engage in reassortment of viral segments, leading to a completely novel influenza virus. It leads to generational pandemics. - If a patient gets a bacterial lobar pneumonia following recent convalescence from influenza infection, USMLE likes <i>S. aureus</i> as a HY cause. The USMLE will not play trivia where they list <i>S. aureus</i> alongside <i>S. pneumo</i> and you're forced to choose. What they'll do is say something about how a guy recently recovered from a viral illness in which he had high fever and myalgias, and now he has a pneumonia caused by a gram-positive coccus in clusters --> answer = <i>S. aureus</i>. In contrast, <i>S. pneumo</i> is gram-positive diplococci. - IM killed vaccine: start age 6 months, then give yearly in the fall or winter throughout life; safe to give during pregnancy. - Intranasal live-attenuated vaccine: ages 2-45; immunocompetent, non-pregnant persons only.
Coronavirus	<ul style="list-style-type: none"> - The virus specifically known as SARS-CoV-2, or COVID-19, caused the 2019 global pandemic. - SARS stands for Severe Acute Respiratory Syndrome. - The pandemic is believed to have started following a laboratory leak in Wuhan, China, although this has been a source of political debate, where initial explanations asserted that there was a natural, zoonotic origin for the virus (i.e., originating from animals, e.g., bats). - Has characteristic spike proteins that create a crown-like appearance on electron microscopy. - The spike proteins bind to ACE2 receptor, allowing for viral fusion with host respiratory epithelium. - Presentation can range from mild respiratory symptoms similar to the common cold (rhinovirus) all the way to severe respiratory disease with multi-organ failure. - Many different vaccine types exist - i.e., mRNA (Moderna; delivers mRNA coding for the spike protein), viral vector (AstraZeneca; delivers mRNA in a harmless viral capsid), and killed (Sinovac; delivers inactivated, killed virus). - Both live viral infection as well as vaccination are known to cause rare adverse effects, such as Bell's palsy and myocarditis, although these effects

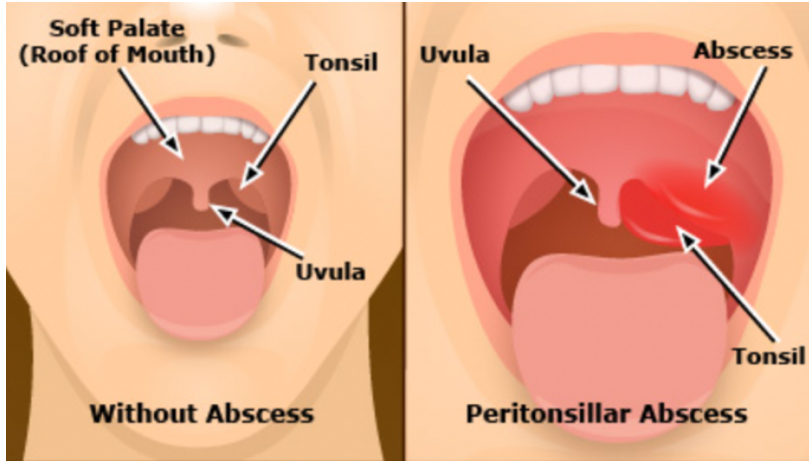
	<p>are not unique to coronavirus and can rarely happen with many viral infections and vaccines.</p> <ul style="list-style-type: none"> - Vaccination mandates and their political implications were (and still are) a source of contentious debate. - Prior to the 2019 pandemic, coronavirus was known to cause SARS in China in 2002 and Middle Eastern Respiratory Syndrome (MERS) in Saudi Arabia in 2012. - Vaccination schedule for children now recommends IM vaccine starting at 6 months; 2-3-doses.
--	--

Vaccine stuff	
<i>S. pneumo</i>	<ul style="list-style-type: none"> - PCV15 at 2, 4, 6 months, then again 12-15 months. - Age ≥ 65: PCV20 once; OR, PCV15 then PPSV23 a year later. - For asplenia/surgical splenectomy, sickle cell, cochlear implant, CSF leak, chronic renal failure/nephrotic syndrome, HIV, and immunosuppressed patients: extra dose of PCV15, followed by PPSV23 8+ weeks later.
Influenza	<ul style="list-style-type: none"> - IM killed vaccine: start age 6 months, then give yearly through life; safe to give during pregnancy. - Intranasal live-attenuated: ages 2-45; immunocompetent, non-pregnant persons.
Coronavirus	- IM vaccine starting at 6 months; 2-3-doses.

HY Pediatric-related respiratory stuff	
Tracheoesophageal fistula (TEF)	<p>- HY pediatric condition in which the proximal esophagus ends in a blind pouch + the distal esophagus connects to the trachea.</p>  <ul style="list-style-type: none"> - Will present as a neonate who coughs up milk with initial feeding. - Highest yield point about TEF is that diagnosis is made via insertion of nasogastric tube (which cannot be inserted fully because it hits the blind pouch of the esophagus). - An NBME Q wants "endoderm" as the abnormal embryology for TEF (makes sense, since esophagus is epithelial lining of the gut \rightarrow endoderm).
Choanal atresia	<ul style="list-style-type: none"> - Weird condition in which the nasal passages don't develop patency, so the neonate is an obligate mouth-breather.

	<div data-bbox="644 203 1302 819" data-label="Image"> </div> <div data-bbox="778 786 874 819" data-label="Caption">Normal</div> <div data-bbox="1046 786 1246 819" data-label="Caption">Choanal Atresia</div> <ul style="list-style-type: none"> - Will present as a child who becomes blue/hypoxic while breast feeding (because he can't breathe through the nose), then cries/becomes pink once detaching from the breast. - Similar to TEF, diagnosis is made via insertion of nasogastric tube. - Part of CHARGE syndrome → Coloboma of the eye (hole in the eye), Hear defects, Atresia of the choanae, Renal defects, Genitourinary anomalies, Ear anomalies.
<p>Congenital diaphragmatic hernia</p>	<ul style="list-style-type: none"> - One of the highest yield Peds conditions on USMLE. - Caused by failure of formation of pleuroperitoneal membranes. - Always occurs on the left, where bowel from the abdomen can herniate up into the left-chest. - Can present as ↓ bowel sounds in the abdomen + ↑ bowel sounds in the left hemithorax. <div data-bbox="667 1323 1286 1928" data-label="Image"> </div> <ul style="list-style-type: none"> - Vignette might say there are cystic-appearing areas in the left hemithorax seen on CXR (loops of bowel).

Neonatal respiratory distress syndrome (NRDS)	<ul style="list-style-type: none"> - Aka hyaline membrane disease. - The answer on USMLE for respiratory distress in kid who is born <34 weeks' gestation. - Due to insufficient surfactant production by type II pneumocytes due to ↓ lamellar bodies (the specialized organelles that produce surfactant). - These kids have ↓ lecithin/sphingomyelin ratio (i.e., <2.0). Normally it is >2-2.4. - Another name for lecithin is dipalmitoyl phosphatidylcholine. This is asked on NBME. - USMLE can give simple vignette of NRDS and then ask for various manipulation of the ratio – i.e., “↑ sphingomyelin” might be an answer (makes sense, since this would ↓ the ratio). - ↓ surfactant production means ↓ alveolar compliance and ↑ elastic recoil. Surfactant is hydrophobic and normally prevents the alveoli from collapsing, so if it's deficient, the hydrophobic interactions of the alveolar walls enable ↑ collapsing/elastic recoil. - CXR shows a “reticulogranular” appearance. Very buzzy and HY. - In order to prevent NRDS, a pregnant woman giving birth <34 weeks' gestation must be two boluses of corticosteroids within 24 hours of parturition, which accelerate fetal lung maturity. For example, there is a 2CK Q where they tell you a woman giving birth at 33 weeks' gestation was given a bolus of corticosteroids 12 hours ago. They ask for next best step → answer = “bolus of corticosteroids.” Sounds weird because they said it was just done, but she needs two boluses. - For management, 2CK wants tactile stimulation first, then place under warming lights. This sequence is HY. Then give exogenous surfactant and oxygen.
Transient tachypnea of the newborn (TTN)	<ul style="list-style-type: none"> - The answer on USMLE when the vignette sounds like NRDS but the kid is term. For instance, they'll say neonate has difficulty breathing, but then you'll notice he's >37 weeks. - Usually seen following C-section or fast vaginal delivery. - Mechanism is insufficient time for the pulmonary lymphatics to clear amniotic fluid from the lungs. - CXR shows “fluid within fissure lines.”
Bronchopulmonary dysplasia	<ul style="list-style-type: none"> - Fibrotic lung disease in an infant caused by continued use of supplemental oxygen. - Vignette will give you a kid who was born at 26 weeks' gestation who was in ICU on oxygen + now is 4 months old and is on home oxygen. They will say ECG shows right-axis deviation +/- CXR shows increased pulmonary vascularity → this reflects RVH (ensuing cor pulmonale) from pulmonary hypertension caused by the bronchopulmonary dysplasia.
Foreign body aspiration	<ul style="list-style-type: none"> - Answer on 2CK for kid under 2 who was crawling around on the floor who now has acute-onset respiratory distress. The vignette will then add one of two features: <ul style="list-style-type: none"> 1) Unilateral hyperresonance in one lung (but not pneumothorax); 2) Unilateral atelectasis + ipsilateral tracheal shift. - Exam will ask for “bronchoscopy,” or “fiberoptic examination of the airways” as the answer.
Allergic rhinitis	<ul style="list-style-type: none"> - Not limited to kids, but can be part of atopy in patients with asthma. - “Cobblestoning” of nasal mucosa is buzzy for allergy. This same word is used to describe the tarsal conjunctiva in allergic conjunctivitis on Peds. - NBME 9 for 2CK has “use of pillow and mattress covers” as the answer. - Otherwise, USMLE wants intra-nasal corticosteroids as first-line med. - USMLE does not want anti-histamines as first-line med.

	<ul style="list-style-type: none"> - 2nd-gen H1 blockers (i.e., loratadine) are the answer if <i>intra-nasal</i> corticosteroids are not listed. Oral prednisone is a wrong answer. - I've seen students choose prednisone and then get irascible and say, "But you said steroids were first-line." → Yeah, bro. Intra-nasal. Not fucking oral.
Adenoid hypertrophy	<ul style="list-style-type: none"> - Just know that enlarged tonsils (adenoids) are a known cause of stridor in pediatrics. Answer = tonsillectomy.
Peritonsillar abscess (Quinsy)	<ul style="list-style-type: none"> - Pus collection causing pain and swelling at posterior oropharynx. - Can be seen as complication of tonsillitis. - Patient can have difficulty opening his/her mouth; this contrasts with bacterial tracheitis, where the patient can fully open his/her mouth (on 2CK NBME, where this detail is important in an otherwise vague vignette). 
Laryngomalacia	<ul style="list-style-type: none"> - Most common cause of stridor in infants. - Softening of airway cartilage. - Vignette will give kid under the age of 1 who has noisy breathing that is mitigated when placed prone (on stomach) or upright. - Self-resolves almost always (i.e., don't treat).
Vascular ring	<ul style="list-style-type: none"> - Weird cause of stridor that USMLE likes to contrast with laryngomalacia. - Vascular embryology variant can lead to airway compression. - In contrast to laryngomalacia, mitigated when neck is extended. - Tx = surgery.
Velopharyngeal insufficiency	<ul style="list-style-type: none"> - High-pitched, hyper-nasal, or whistling speech in patients with Hx of cleft palate due to shortened palate, with or without repair. - It's the answer on a 2CK NBME, so know that it exists. They will simply just give you vignette of cleft palate + ask what the kid is at risk for.
Cholesteatoma	<ul style="list-style-type: none"> - Idiopathic squamous proliferation in middle ear behind the tympanic membrane that presents as an enlarging mass. - Can cause obstructive hearing loss + grow into inner ear. - Requires surgery. - Sounds like an obscure diagnosis, but it's not. Be aware it exists for Peds.
Tracheomalacia	<ul style="list-style-type: none"> - Not pediatric, but I'm putting it here because I see this confused with laryngomalacia. - This is a cause of stridor in (usually) adults who have stridor developing months post-surgery. - Caused by Hx of intubation leading to softening of airway cartilage. - Just know this diagnosis / it exists + don't confuse with laryngomalacia.

Differentiating viral vs bacterial URTI

- The CENTOR criteria are exceedingly HY for IM.

- If 0 or 1 point, the URTI is unlikely to be bacterial (i.e., it's likely to be viral). If 2-4 points, the chance is much greater that the URTI is bacterial.

- **1) Absence of** cough (i.e., no cough = 1 point; if patient has cough = 0 points).
- **2) Fever** >38 C.
- **3) Tonsillar exudates.**
- **4) Lymphadenopathy** (cervical, submandibular, etc.).

- There is a version of the criteria that includes age, but on the USMLE it can cause you to get questions wrong. So just use the simplified above four points.

- If 0-1 point, answer = "supportive care"; or "no treatment necessary"; or "warm saline gargle" (same as supportive care); or "acetaminophen." Latter is answer for 3M with viral URTI + fever on NBME form.
- If 2-4 points, next best step = "rapid Strep test." If rapid Strep test is negative, answer = throat culture, **NOT** sputum culture.
- While waiting on the throat culture results, we send the patient home with amoxicillin or penicillin for presumptive Strep pharyngitis.
- If child is, e.g., 12 years old, and develops a rash with the beta-lactam, answer = beta-lactam allergy.
- If the vignette is of a 16-17 year-old who has been going on dates recently (there will be no confusion; the USMLE will make it clear) + gets a rash with the beta-lactam, the answer = EBV mononucleosis; therefore do a heterophile antibody test (Monospot test).
- **EBV is the odd virus out that usually presents with all four (+) CENTOR criteria and presents like a bacterial infection.**
- This is why it's frequently misdiagnosed as Strep pharyngitis. It is HY to know that beta-lactams given to patients with EBV may cause rash via a hypersensitivity response to the Abx in the setting of antibody production to the virus. EBV, in a patient who does not receive Abx, can cause a mild maculopapular rash. But the rash with beta-lactam + EBV causes a more intense pruritic response generally 7-10 days following Abx administration on the extensor surfaces + pressure points.

Ventilator settings nonsense

- Students will sometimes nag about pedantic ventilator settings info. The vast majority of it is garbage for USMLE. What I can basically say is that **increasing PEEP** (positive-end expiratory pressure) is probably the answer 4 out of 5 times for any ventilator settings-type of question. The Q might give you a big 15-line rambling paragraph where you're not sure what's going on, and then the answer is just "increase PEEP."

- PEEP keeps the alveoli open longer, thereby facilitating gas exchange.

- When the patient is on a ventilator, the general aims are:

- Keep FiO₂ as low / as close to room air as possible (i.e., high O₂ can cause free radical damage);
- Keep tidal volume as low/normal as possible (i.e., 400-500-ish mL); high tidal volumes can cause ventilator-associated barotrauma.
- Increase PEEP if it means lower FiO₂ and tidal volumes can be achieved.

- But the above needs to be taken with a caveat. For example, the Q might say the patient is on a ventilator and has arterial pO₂ of 40 mm Hg (normal is 80-100) + FiO₂ is 100% + tidal volume is 1000 mL, and the answer will be "increase PEEP." The student says, "Wait but I thought you said we want to reduce FiO₂ and tidal volume." → Sure, but we can't do that here because pO₂ is super-low, so that would only exacerbate it further.

- As I talked about for ARDS earlier, you could be aware the triad of 1) prone positioning, 2) low-tidal volume mechanical ventilation, and 3) permissive hypercapnia can be implemented.

- A very HY point is that ↓ CO₂ causes ↓ cerebral perfusion (this is why patients faint in panic attacks, which is asked on NBME). The first step in managing ↑ intracranial pressure is "intubation + hyperventilation."

- They also ask the inverse of this on NBME – i.e., they say an anesthesiologist wants to \uparrow a patient's cerebral perfusion, and the answer is "decrease respiratory rate" \rightarrow causes \uparrow CO₂ \rightarrow \uparrow cerebral perfusion.
- Ventilator-acquired pneumonia (VAP) should be treated with vancomycin PLUS either ceftazidime or cefepime. Vancomycin not only covers MRSA but also is effective against some high-resistance *S. pneumo* strains. Ceftazidime (3rd generation ceph) and cefepime (4th gen ceph) are very effective against *Pseudomonas*, which is a HY nosocomial organism for VAP.
- Patients should ideally be weaned from ventilators as quickly as possible. USMLE also likes patients who are sick on ventilators as sometimes having euthyroid sick syndrome – i.e., they will say patient cannot be weaned from ventilator + has \downarrow T₃ and normal TSH \rightarrow answer = euthyroid sick syndrome. The full array of arrows are: \downarrow T₃, \uparrow rT₃, \leftrightarrow T₄, \leftrightarrow TSH. If you have no idea what I'm talking about, then I recommend going through my HY Arrows PDF.
- If a patient ever has a high CO₂ (NR 33-44 mmHg) \rightarrow answer can = "ventilatory insufficiency." This applies to both patients on and off ventilators. Don't be confused if they give you \uparrow respiratory rate. New NBME form gives RR of 40 with \uparrow CO₂ as an example. Sometimes patients have shallow breathing despite \uparrow RR.

HY Pulmonary drug points	
Bosentan	<ul style="list-style-type: none"> - Endothelin-1 receptor antagonist used for pulmonary hypertension. - Endothelin is a vasoconstrictor \uparrow in pulmonary hypertension. - There is an NBME Q where guy is shaving + cuts himself + they ask what will be seen at site of injury \rightarrow answer = \uparrow endothelin. So be aware that even though 14/15 times this relates to pulmonary vascular constriction, it is technically a vasoconstrictive mediator not isolated to the lungs.
Methotrexate	<ul style="list-style-type: none"> - Dihydrofolate reductase inhibitor. - 1st-line DMARD for RA + 1st-line oral agent for psoriasis that fails topicals. - Causes pulmonary fibrosis (and hepatotoxicity and neutropenia). - Toxicity can be mitigated with "leucovorin rescue," aka folinic acid (not folic acid).
Albuterol	<ul style="list-style-type: none"> - Short-acting β2-agonist used for asthma. - Can cause tremor (asked on NBME).
Fluticasone, Beclomethasone	<ul style="list-style-type: none"> - Inhaled corticosteroids (ICS) used for asthma and COPD. - Used for prevention / to decrease recurrence of episodes. They have no role in acute exacerbations. For the latter, IV methylprednisolone is used.
Prednisone	<ul style="list-style-type: none"> - Most effective at \downarrow recurrent asthma attacks, but used last resort because oral steroids can cause Cushing syndrome and growth stunting.
Montelukast, Zafirlukast	<ul style="list-style-type: none"> - Leukotriene receptor antagonists (LTC, D, and E₄). - Leukotrienes normally cause bronchoconstriction. So these agents \downarrow airway constriction. - LTB₄ is special and is a neutrophilic chemotactic molecule. For immuno, you can memorize that LTB₄, IL-8, and C5a are HY neutrophilic chemotactic molecules. - Can be used for asthma in patients with aspirin-induced asthma (blockage of COX shunts arachidonic acid down the lipoxygenase pathway toward leukotrienes), or for asthma in general in between a LABA and prednisone.
Zileuton	<ul style="list-style-type: none"> - Lipoxygenase inhibitor. Blocks synthesis of leukotrienes. - Use-case same as the -lukasts.
Nedocromil, Cromolyn sodium	<ul style="list-style-type: none"> - Mast cell stabilizers used for asthma. Prevent release of histamine.
Tiotropium	<ul style="list-style-type: none"> - Long-acting muscarinic receptor antagonist (LAMA) used first-line for COPD.
Olodaterol	<ul style="list-style-type: none"> - Long-acting β2-agonist (LABA) used first-line for COPD. - As discussed earlier, either a LAMA or LABA can be used first-line for COPD.
Ipratropium	<ul style="list-style-type: none"> - Short-acting muscarinic receptor antagonist (SAMA) used for COPD. - Not first-line anymore, but still shows up on 2CK material as an agent that's used. Some old-school practitioners still use it, so don't disregard it.
Epoprostenol	<ul style="list-style-type: none"> - PGI₂ prostacyclin that can be used for pulmonary hypertension.
Sildenafil	<ul style="list-style-type: none"> - Viagra; PDE-5 inhibitor that can also be used for pulmonary hypertension.

Nifedipine	<ul style="list-style-type: none"> - Dihydropyridine calcium channel blocker that can be used for pulmonary HTN. - As discussed in the Cardio PDF, can cause peripheral edema/fluid retention.
Omalizumab	<ul style="list-style-type: none"> - Monoclonal antibody against IgE. - Can be used in theory in severe asthmatics who have high IgE levels.
Dornase alfa	<ul style="list-style-type: none"> - Nucleotidase used to break down airway mucous in cystic fibrosis patients.
Guaifenesin	<ul style="list-style-type: none"> - Mucolytic agent that softens mucous in cystic fibrosis.
Ivacaftor	<ul style="list-style-type: none"> - Helps localize CFTR channel to membrane and correct its folding (in CF clearly).
Pirfenidone	<ul style="list-style-type: none"> - Used for idiopathic pulmonary fibrosis. - Anti-fibrotic agent that inhibits TGF-β-mediated collagen synthesis.

IM Renal

Basic HY Renal lab values for IM	
Blood urea nitrogen (BUN)	<ul style="list-style-type: none"> - Should be <20 mg/dL. - High urea nitrogen in the blood is called azotemia. - "Uremia" technically means "urea in the blood," but is used to refer to patients who have symptomatic renal failure with poor lab values. This has absolutely zero to do with hyperuricemia (gout) and is sometimes confused by students.
Creatinine (Cr)	<ul style="list-style-type: none"> - 0.7-1.2 mg/dL - Once you've hit a creatinine of 2, you've lost ~90% of your renal function.
Potassium (K ⁺)	<ul style="list-style-type: none"> - 3.5-5.0 mEq/L. - Will always be elevated in renal failure on USMLE. - This is because the kidney normally secretes (i.e., excretes through tubular walls into the urine) K⁺ in the cortical collecting duct under the action of aldosterone. So if the kidney is fucked up, we can't do that, so serum K⁺ rises.
Sodium (Na ⁺)	<ul style="list-style-type: none"> - 135-145 mEq/L. - Can be variable in renal failure as per my observation on NBMEs. - Aldosterone normally reabsorbs sodium in the cortical collecting duct in exchange for potassium being secreted, so one might think it should automatically be low if the kidney can't reabsorb it. But the kidney has a multitude of sodium regulation mechanisms (i.e., vasopressin), so Na⁺ can be normal.
Calcium (Ca ²⁺)	<ul style="list-style-type: none"> - Always ↓ in renal failure. This is due to 2 reasons: <ol style="list-style-type: none"> 1) Ca²⁺ is normally reabsorbed in the late-distal convoluted tubule (DCT), so if we can't do that, serum Ca²⁺ falls. 2) Proximal convoluted tubule (PCT) of the kidney is normally where 1α-hydroxylase, under the action of PTH, activates inactive 25-OH-D3 into active 1,25(OH)₂-D3. The latter then goes to the small bowel, where it ↑ absorption of Ca²⁺. So if we can't do that, serum Ca²⁺ falls. - Low serum Ca²⁺ means ↓ negative feedback at the Ca²⁺-sensing receptors at the parathyroid glands → PTH goes up. We call this secondary hyperparathyroidism, which means PTH is high due to a cause external to the parathyroid glands themselves. You need to know secondary hyperthyroidism is due to renal failure.
Phosphate (PO ₄ ³⁻)	<ul style="list-style-type: none"> - Always ↑ in renal failure. - This is for 2 reasons: <ol style="list-style-type: none"> 1) The kidney cannot filter it out sufficiently. Lots of phosphate is normally filtered by healthy kidneys. 2) PTH normally acts to ↓ phosphate reabsorption in the PCT via downregulation of 3 different types of phosphate pumps. Since the function of PTH is impaired, the kidney <i>reabsorbs too much</i> phosphate, so serum levels rise. - Combo of ↓ Ca²⁺ and ↑ PO₄³⁻ in renal failure = secondary hyperparathyroidism.
Bicarbonate (HCO ₃ ⁻)	<ul style="list-style-type: none"> - Always ↓ in renal failure. - This is for 2 reasons: <ol style="list-style-type: none"> 1) The kidney cannot reabsorb bicarb in the PCT as well, so ↑ bicarb in the urine → ↓ bicarb in serum → metabolic acidosis. 2) The kidney cannot secrete protons (H⁺) in the cortical collecting duct as readily → retention of H⁺ mops up HCO₃⁻ → ↓ serum bicarb. - Renal failure = Uremia = the U in MUDPILES for high anion-gap metabolic acidoses. (If you need help on the acid-base stuff, do my HY Arrows PDF).

Afferent vs efferent regulation	
Afferent arterioles	<ul style="list-style-type: none"> - Go to the kidney. - Patency maintained by vasodilating prostaglandins. - NSAIDs inhibit prostaglandin synthesis → ↓ dilation of afferent arterioles → ↓ renal blood flow. - NSAIDs don't actively constrict the afferent arterioles. This is incorrect wording. They just merely ↓ vasodilation / ↓ diameter of the afferent arterioles.
Efferent arterioles	<ul style="list-style-type: none"> - Leave the kidney. - Angiotensin II normally constricts these. - ACEi/ARBs therefore ↑ diameter of the efferent arterioles. They are not dilating them; they are merely ↓ constriction of them. As mentioned above, prostaglandins will actively dilate the afferent arterioles. - Some students might say, "Well doesn't AT II act on the afferent arterioles as well?" In theory, a very minor amount, but on USMLE, this will get you questions wrong. You want to think:
Summary	<p>AT II = constricts efferent; ACEi/ARBs = ↓ constriction of efferent (↑ diameter). Prostaglandins = dilate afferent; NSAIDs = ↓ dilation of afferent (↓ diameter).</p>

Pre-, intra-, and post-renal azotemias	
BUN/Cr, FENa	<ul style="list-style-type: none"> - BUN/Cr = Blood urea nitrogen to creatinine ratio. - FENa = fractional excretion of sodium (i.e., amount of sodium in the urine). - There's no "normal" range you should be looking for here for either of these. - What matters is that when there is an actual kidney problem, we look at the values to help us figure out what the diagnosis is. But we never actually say, "Oh the BUN/Cr or FENa is out of the normal range." - BUN/Cr >20 and FENa <1% mean pre-renal azotemia. - BUN/Cr <20 and FENa >1% just simply mean "not pre-renal." - The notion of intra- vs post-renal having slightly different ranges is nonsense for USMLE. - Also, what I've come to learn from NBME Qs is that only ~9/10 times the BUN/Cr will be what we expect. There are a couple 2CK NBME Qs that give BUN/Cr <20 for pre-renal azotemia and >20 for acute tubular necrosis. If the NBME ever "breaks the rules" this way, the vignette will be overwhelmingly obvious what the diagnosis is anyway.
Pre-renal	<ul style="list-style-type: none"> - Pre-renal azotemia means there is renal pathology because of reduced renal blood flow over the sub-acute to chronic time frame. The kidney will do everything it can to ↑ retention of fluid (because it thinks blood volume is low). The way it accomplishes this is by ↑ reabsorption of urea and sodium, since water will follow. This is why blood <i>urea</i> nitrogen is high (i.e., BUN/Cr >20) and sodium in the urine is low (FENa <1%). - Notice above I stress <i>sub-acute to chronic time frame</i> (i.e., days-months), since one of the highest yield points you need to know for USMLE is that <i>acute</i> ↓ perfusion (i.e., seconds to minutes) to the kidney from blood loss, acute heart failure exacerbation, or arrhythmia (i.e., VFib for 30 seconds before resusc) causes acute tubular necrosis, not pre-renal. - This is all over the NBME exams. For example, if they say a guy loses lots of blood during surgery and receives 20 packs of RBCs, then two days later while recovering in hospital he gets oliguria + deterioration of renal function, the answer is acute tubular necrosis, not pre-renal. Student says, "Wait, but there was ↓ renal perfusion though, so how does that make any sense. Isn't pre-renal caused by ↓ perfusion?" → <i>The PCT of the kidney is the most susceptible to anoxic/hypoxic injury due to the ↑ concentration of ATPase transporters. So acute ↓ drop in blood flow → acute hypoxia → PCT sheds.</i> - There is a 2CK NBME Q where they mention a guy post-op who had <i>not</i> lost any blood during surgery + had <i>not</i> experienced any episodes of low BP + was started on ketorolac (an

	<p>NSAID) for pain post-op + now has oliguria and ↑ creatinine → answer = “hypoperfusion” as cause; this is example of where NSAIDs, not ATN, can cause post-op oliguria from pre-renal.</p> <ul style="list-style-type: none"> - HY causes of pre-renal for USMLE are NSAID or diuretic use, chronic left heart failure, or dehydration from days of vomiting/diarrhea. - USMLE will give patient who’s been on an NSAID (e.g., naproxen) for several weeks, or who was commenced on furosemide (loop diuretic) a few days ago. - Vignette can give patient who is on an NSAID + now has peripheral edema + they ask why there’s edema → answer = “↓ renal excretion of sodium.” This is because the PCT ↑ reabsorption of sodium in pre-renal (FENa <1%). They will also sometimes give NSAID + edema + ask what you do, and the answer is just “discontinuation of ibuprofen.”
Intra-renal	<ul style="list-style-type: none"> - Essentially synonymous with acute tubular necrosis on USMLE. - The kidney can’t reabsorb urea and sodium as easily, so BUN is lower (i.e., BUN/Cr is <20) and sodium is higher in the urine (i.e., FENa is >1%). - I discuss acute tubular necrosis in more detail in its own table below, but as I mentioned above in red font, the most important point for USMLE is that you remember <i>acute</i> drop in perfusion to the kidney causes acute tubular necrosis, <i>not</i> pre-renal. I need to be an asshole and inculcate that.
Post-renal	<ul style="list-style-type: none"> - Almost always due to BPH on USMLE, but can also be due to ovarian or cervical cancer impingement on the ureter(s). - What you need to know is: old dude + high creatinine = BPH till proven otherwise. - The answer on USMLE is often just “increased Bowman capsule hydrostatic pressure.” - Next best step is “insertion of catheter” to relieve the urinary retention, even if the patient has bacteriuria (i.e., choose catheter insertion over antibiotics). - Another 2CK Q has “check post-void volume” as answer in elderly male with high Cr. USMLE won’t force you to choose between catheter insertion of checking post-void volume. - Normal post-void volume is <50ish mL. If the USMLE wants overflow incontinence, they’ll give post-void volume ~300-400+ mL. - Diabetic neurogenic bladder (i.e., hypotonic bladder from neuropathy to the detrusor muscle) can also lead to overflow incontinence and post-renal azotemia, but as I said, most Qs on USMLE will focus on the old dude with BPH. - Hydronephrosis can be seen as large, dilated kidneys in patients with obstruction, but this is rare diagnosis.

Nephritic vs Nephrotic syndromes

- Nephritic conditions have blood in the urine; nephrotic syndromes don’t.
- You need to memorize for USMLE which HY conditions are nephritic vs nephrotic. Don’t worry, I keep things real clean and concise in the tables below without the bullshit nonsense of other resources.
- There are four main points you should memorize as being part of each syndrome type.

Nephritic syndromes:

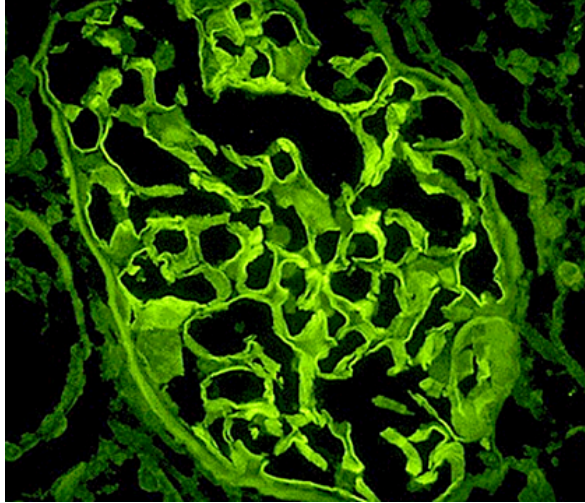
- 1) **Hematuria** (blood in the urine).
- 2) **Oliguria** (↓ urinary output; the definition is <400 mL/day, but USMLE won’t assess that number).
- 3) **Azotemia** (↑ blood urea nitrogen; this is because urinary output is ↓).
- 4) **Hypertension** (↑ RAAS due to inflammation of renal microvasculature).

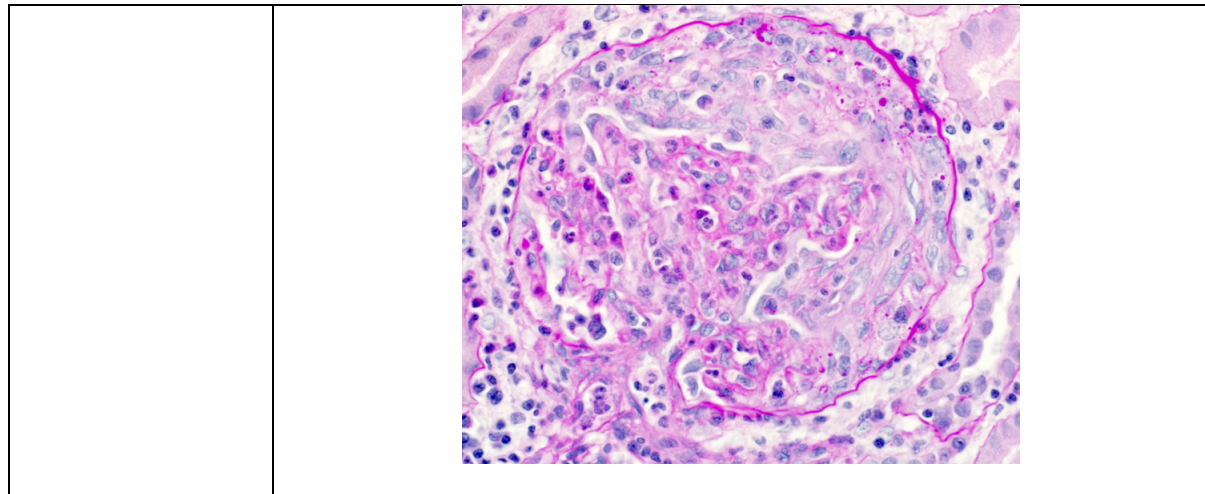
Nephrotic syndromes:

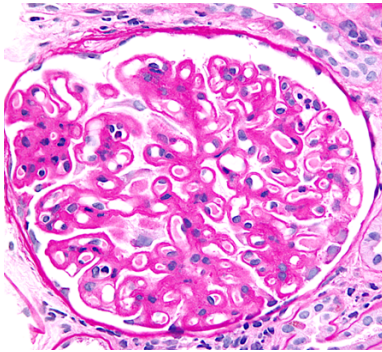
- 1) **Proteinuria** (nephrotic level by definition is >3.5g/day, but USMLE won’t assess that number).
- 2) **Hypoalbuminemia** (due to the proteinuria; will be <3.5 g/dL, but USMLE doesn’t care about the #).
- 3) **Peripheral edema** (due to the hypoalbuminemia → ↓ serum oncotic pressure → transudation of fluid into interstitial spaces; severe can present with ascites; if the stem says “pre-sacral edema,” this is nephrotic syndrome till proven otherwise on USMLE).
- 4) **Hyperlipidemia** (liver pumps out apolipoproteins in an attempt to preserve serum osmolality / oncotic pressure).

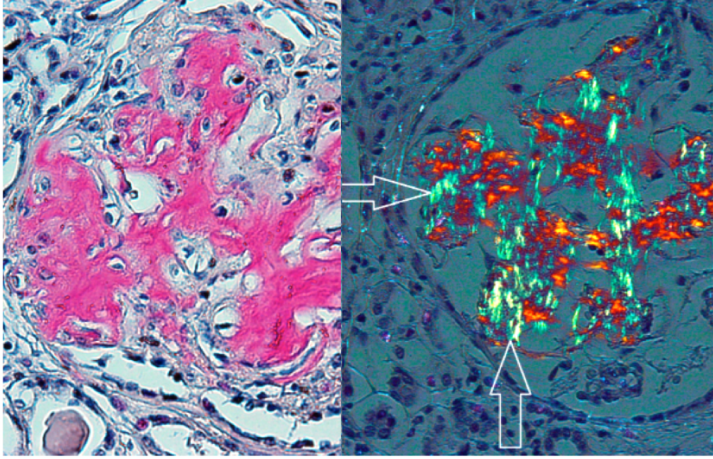
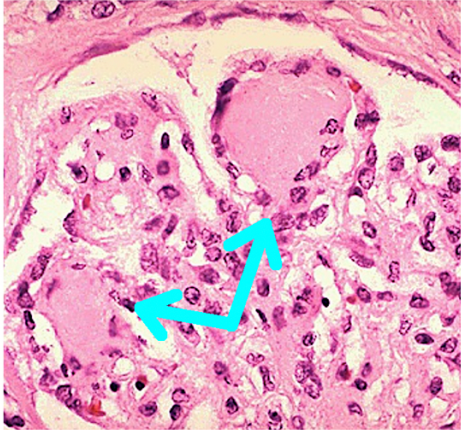
- Should be noted that nephritic syndromes often have proteinuria, just usually not at nephrotic levels. Students sometimes erroneously think nephritic syndromes don't have proteinuria because it's not part of the 4-point categorization above.
- You don't have to worry about the notion of which conditions are "both nephritic and nephrotic." What is most important is: simply know which conditions have hematuria and which ones don't (via tables below).
- Nephrotic syndromes can ↑ risk of DVT, renal vein thrombosis, and varicocele due to loss of antithrombin III in the urine → hypercoagulable state. This is because nephrotic syndrome usually entails non-specific massive protein loss due to loss of size and charge barrier, and antithrombin is a protein. The NBME wants you to know left renal vein thrombus accretion from hypercoagulable state can cause varicocele.

HY Nephritic syndromes	
PSGN	<ul style="list-style-type: none"> - Post-streptococcal glomerulonephritis; aka "proliferative glomerulonephritis"; the latter is asked on NBME, where they give vignette of PSGN, and answer is just "proliferative glomerulonephritis." Student is like what the hell? - Aka "proliferative glomerulonephritis" (asked on NBME, where they give vignette of PSGN, and answer is just "proliferative glomerulonephritis"). - Answer can sometimes be written by NBME as just "acute glomerulonephritis." - The answer on USMLE for red urine 1-3 weeks following a sore throat caused by Group A Strep (<i>Strep pyogenes</i>). This is in contrast to IgA nephropathy (which I discuss in detail below), which is red urine 1-3 days following a sore throat. - PSGN can be caused by skin infections. This can be impetigo (school sores), cellulitis, or erysipelas (I discuss these in detail in my HY Derm PDF). For example, the Q might say a 10-year-old has yellow crusties on his arm for the past 7 days (impetigo) + now has red urine → answer = "acute glomerulonephritis." - Type III hypersensitivity (antigen-antibody complexes that form in blood and deposit in the kidney). Don't confuse with rheumatic heart disease, which is a type II HS. - Serum complement protein C3 can be ↓ (can also be ↓ in SLE, but unrelated). - Streptolysin O or A titers will be ↑. - PANDAS is tested on 2CK → Pediatric Autoimmune Neuropsychiatric Disorder Associated with <i>Streptococci</i> → presents as new-onset tic/Tourette, OCD, or ADHD within weeks of Group A Strep infection. - Descriptors such as subepithelial deposits or "lumpy bumpy" appearance on electron microscopy (EM), etc., have been parroted across resources over the years but are essentially garbage for USMLE. - PSGN usually self-resolves in kids without sequela. But USMLE wants you to know that ↑ age is means worse prognosis, where chance of renal failure is ↑ if it occurs in adults. This is probably related to the more robust immune response resulting in more advanced renal damage.
IgA nephropathy	<ul style="list-style-type: none"> - Aka Berger disease; IgA deposition in renal mesangium. - Red urine 1-3 days after a sore throat. This is in contrast to PSGN, which is red urine 1-3 weeks after a sore throat. I just mentioned it above obviously. But students fuck this up despite the inculcation so I'm reiterating it like an asshole. - Caused by viral infection, not Group A Strep. - Can sometimes be caused by GI infections, but USMLE usually avoids this etiology unless including it in the Henoch-Schönlein purpura constellation. - Henoch-Schönlein purpura is classic tetrad: <ol style="list-style-type: none"> 1) Palpable purpura (usually on buttocks/thighs). 2) IgA nephropathy (red urine). 3) Arthralgias. 4) Abdominal pain. - All 4 need not be present for HSP, but the abdo pain component here is presumably viral gastroenteritis leading to IgA nephropathy.

Goodpasture syndrome	<ul style="list-style-type: none"> - The answer on USMLE for a male 20s-40s with hematuria and hemoptysis. Similar to Wegener and microscopic polyangiitis, can cause RPGN. - Caused by anti-glomerular basement membrane antibodies (anti-GBM), which are antibodies against collagen IV. - Renal biopsy will show linear immunofluorescence. USMLE likes showing the bright green image for this.  <ul style="list-style-type: none"> - Do not confuse this with Alport syndrome, which is an XR condition caused by mutations in collagen IV.
Alport syndrome	<ul style="list-style-type: none"> - X-linked disease; <i>mutation in collagen IV gene</i>. - Do not confuse with Goodpasture syndrome, which is antibodies against type IV collagen. - The answer on USMLE for a male who has red urine + an eye or ear problem (collagen IV is present in basement membranes in the kidney, ear, and eyes). - The “eye problem” can be blurry vision/cataracts; the “ear problem” will be neurosensory hearing loss (due to organ of Corti dysfunction). - Some students have asked if it’s XR or XD. Literature appears to be varied, but USMLE doesn’t care. On offline NBME 18, however, it’s mentioned in a Q as XR. - You can memorize “splitting of the lamina densa” as associated with Alport.
MPGN	<ul style="list-style-type: none"> - Membranoproliferative glomerulonephritis. - The answer on USMLE for red urine in a patient with hepatitis C, heroin use, or malignancy. - Descriptors such as “dense deposits,” “C3 nephritic factor” and “duplication of basement membranes” are all basically nonsense for USMLE. - Answer is “renal biopsy” as the next best step. This guides our management. - A 2CK IM form has “heroin” as the answer (heroin-induced nephropathy) for patient with protein and blood in the urine. In contrast, FSGS (discussed below) from heroin has no blood in the urine.
DPGN	<ul style="list-style-type: none"> - Diffuse proliferative glomerulonephritis. - The answer on USMLE for red urine in a patient with SLE. - Can sometimes be associated with “wire-looping of capillary walls.” - Same as with MPGN, USMLE wants “renal biopsy” as the next best step, since this guides our management.
RPGN	<ul style="list-style-type: none"> - Rapidly progressive glomerulonephritis. - Acute deterioration in renal function in the setting of a vasculitis (i.e., Wegener, microscopic polyangiitis) or Goodpasture syndrome. I discuss these conditions in detail later in this PDF, don’t worry. - Characterized by fibrin crescents on biopsy.



HY Nephrotic syndromes	
Minimal change disease	<ul style="list-style-type: none"> - The answer on USMLE for otherwise unexplained edema in a kid who doesn't have blood in the urine. - Presents as peripheral edema, periorbital edema, and/or ascites. - Almost always this is pediatric. Very rarely it can be due to Hodgkin in adult. - Classically post-viral (i.e., URTI), but ~50% of vignettes won't mention that. - In other words, textbook vignette is an 8-year-old who has the sniffles for 4 days, followed by peripheral and periorbital edema a week later, without blood in the urine. Once again though, the stem need not mention the viral infection. - Called minimal change disease because light microscopy (LM) shows no abnormalities. EM, however, shows effacement of the podocytes. - Mechanism for nephrotic syndrome is "loss of size and charge barrier." - Corticosteroids are the treatment and are highly effective. - A 2CK Q gives minimal change disease as etiology for spontaneous bacterial peritonitis (i.e., any cause of ascites can cause SBP; I discuss this stuff in the GIT PDF in extensive detail). - MCD is aka lipid nephrosis (lipid droplets can be seen in urine on LM).
Membranous glomerulonephritis / nephropathy	<ul style="list-style-type: none"> - The answer on USMLE for nephrotic syndrome in patient who has: <ul style="list-style-type: none"> - Exposure to drugs: dapsone, gold salts, sulfonamides. - Infection: hepatitis B (Hep C can cause it too, but rare). - Visceral cancers, e.g., breast, pancreatic. - Autoimmune (primary): antibodies against phospholipase A2 receptor. - The LM image is important and shows highly eosinophilic (pink) and inflamed / thickened capillary walls. 
Renal amyloidosis	<ul style="list-style-type: none"> - Can cause "spike and dome" appearance of subepithelial deposits on EM. - The answer on USMLE for nephrotic syndrome in multiple myeloma.

	<ul style="list-style-type: none"> - Amyloidosis means protein depositing where it shouldn't be depositing. - Multiple myeloma = cancer of plasma cells that produce too much immunoglobulins → high serum IgG kappa/lambda light chains. Immunoglobulins are proteins → these fly through the kidney and cause Bence-Jones proteinuria; they also deposit in the renal parenchyma, causing renal amyloidosis. - Biopsy shows classic apple-green birefringence with Congo red stain.  <ul style="list-style-type: none"> - For some magical reason, USMLE cares you know that the amyloid appears this way because it is β-pleated sheets (i.e., answer on NBME; α-helices is wrong); makes sense since the former are "flat" and can reflect light at different angles. - An NBME Q has "renal parenchymal disease" as answer for kidney issue due to multiple myeloma.
<p>Diabetic glomerulosclerosis</p>	<ul style="list-style-type: none"> - Diabetes is the most common cause of chronic renal failure. - Renal failure simply means ↓ glomerular filtration rate (GFR). - USMLE wants the first two changes that occur in the kidney due to diabetes as follows: <ol style="list-style-type: none"> 1) Hyperfiltration (↑ glucose crossing the glomerular basement pulls water with it → polyuria). Sometimes the Q can just simply give you diabetes + they ask what's most likely to be seen initially → answer = "↑ glomerular filtration." Over time, the kidney will fail and GFR will ↓. 2) Thickening of the glomerular basement membrane (non-enzymatic glycosylation of the membrane → loss of size and charge barrier). - Kimmelstiel-Wilson nodules are composed of hyaline and look like pink circles on light microscopy. This image is very HY. 

	<ul style="list-style-type: none"> - Hyaline arteriosclerosis is deposition of hyaline (protein) in the walls of the renal vasculature. Although this can be due to many things, on USMLE, they want you to know this is caused by diabetes. - ACEi (e.g., lisinopril) or ARBs (e.g., valsartan) are the first drugs used in diabetes if there is HTN (>130/80 in diabetes, not 140/90), proteinuria, or ↑ creatinine or renin. - AT-II normally constricts efferent arterioles leaving the kidney, causing a backup of pressure at the glomerulus. This serves the purpose of maintaining GFR (i.e., filtration through Bowman capsule) when renal blood flow has ↓. - In other words, when renal perfusion ↓, RAAS goes ↑, AT-II goes ↑, and we get constriction of efferent flow leaving the kidney → ↑ filtration fraction (GFR/renal plasma flow), where we have GFR staying the same despite ↓ perfusion. - ACEi/ARBs ↓ constriction of efferent arterioles (they don't "dilate"; this refers to the action of prostaglandin on the afferent arterioles going to the kidney), thereby ↓ filtration fraction and reducing GFR. This might sound like a bad thing – i.e., "Why would we want to ↓ GFR in diabetes if it's the most common cause of chronic renal failure?" → The answer is because the slightly reduced GFR and filtration fraction early on ↓ the rate at which excess glucose is filtered across the glomerulus. Over time, it is inevitable that the glomerular basement membrane will non-enzymatically glycosylate and thicken, so ACEi/ARBs slow this process (i.e., slightly reduce GFR early in order to prevent a massive decrease later).
Focal segmental glomerulosclerosis (FSGS)	<ul style="list-style-type: none"> - The answer on USMLE for nephrotic syndrome in sickle cell. - Can also be caused by heroin and HIV. - Not as responsive to steroids as MCD. - FSGS literally means "some parts of some nephrons are affected." <ul style="list-style-type: none"> - Focal = some glomeruli. - Diffuse = all glomeruli. - Segmental = part of nephron. - Global = all of nephron.

Acute tubular necrosis	
<ul style="list-style-type: none"> - Sloughing of PCT tubular epithelial cells due to chemical or ischemic insult. - Only ~50% of Qs will mention "muddy brown granular casts," or "dirty brown granular casts," or "brown, pigmented casts." - The other ~50% of Qs will just mention oliguria or acutely worsening renal function in patient with classic ATN etiologies. <p>Next best step in diagnosis (answer on 2CK form) is "measurement of urine sodium and creatinine concentrations." We expect FENa >1% and BUN/Cr <20 almost always for ATN.</p>	
Cause	HY points
Drugs	<ul style="list-style-type: none"> - Can be caused by drugs: aminoglycosides (gentamicin, tobramycin, amikacin); cisplatin (a chemo agent), or IV contrast. - Any of the above drugs + new-onset oliguria or ↑ creatinine (there need not be mention of casts) = ATN. - For instance, new NBME simply tells you patient was given many drugs and now has creatinine of 2 (NR 0.1-1.2) + no mention of casts + they ask for what was given → answer = gentamicin. Not hard. - Patient who's recently been treated for endocarditis + now has new-onset oliguria = ATN due to gentamicin (empiric Tx for endocarditis = gentamicin + vancomycin [new literature suggests vancomycin is not reliably nephrotoxic]). - Contrast nephropathy is exceedingly HY on 2CK, where they want you to know that adequate hydration prior to IV contrast is the number-one way to prevent it. For instance, they'll say patient got a CT + now has ↑ creatinine + they'll ask how it could have been prevented → answer = "0.9% saline," or just "IV hydration therapy."
Rhabdomyolysis	<ul style="list-style-type: none"> - Myoglobin is nephrotoxic. Big risk factors are alcoholism, falls, intense training (e.g., marathon), McCordle syndrome, statins/fibrates.

	<ul style="list-style-type: none"> - Rhabdo causes a false (+) blood on urine dipstick. They will say urinalysis shows 2+ blood but only 1-2 RBCs/hpf. This is because the dipstick can't differentiate between free myoglobin and hemoglobin on RBCs. - One Surgery Q gives 3-4 RBCs/hpf as negative. I've seen this fool some students who were already aware of the false (+) blood point about rhabdo. If the Q wants (+) RBCs, they'll say like 10-20+/hpf. - The other half of rhabdo vignettes won't mention the false (+) urinalysis and will instead just say oliguria. You need to know that refers to ATN. - For example, an NBME-favorite vignette is patient being found at bottom of stairs in his/her house + has false (+) blood on urine dipstick and/or oliguria → answer = rhabdomyolysis. - They also like ↑ K⁺ as part of rhabdo vignettes (makes sense if we have renal failure from ATN) and ↑ serum creatine kinase (CK). - Q can say 44-year-old guy found on bench in park has ↑ K⁺, ↑ CK, and oliguria → diagnosis = rhabdo. Or they'll say just ↑ CK + oliguria, and they ask what is most likely to be seen in this guy → answer = ↑ K⁺.
Acute ischemia	<ul style="list-style-type: none"> - It's to my observation acute ischemia is the highest yield cause of ATN on NBME exams. - Even though the medulla of the kidney technically receives less blood flow compared to the cortex, as I mentioned earlier, the USMLE is obsessed with the PCT of the kidney as most susceptible to anoxic / hypoxic injury. This is due to the ↑ concentration of PCT ATPase transporters, so acute ↓ drop in blood flow → acute hypoxia → PCT sheds. - NBME loves <i>cellular swelling</i> as part of this mechanism – i.e., acute ischemia → ↓ activity of PCT ATPases → buildup of intracellular Na⁺ → water stays with sodium → tubular cell swelling. Answer on NBME for why there's swelling simply = ↓ ATPase activity (this is similar mechanism for why we get swelling + hemolysis in pyruvate kinase deficiency). - Acute ischemia to the kidney can be due to loss of blood from trauma/surgery, acute arrhythmia (e.g., 30 seconds of Vfib), MI, or acute exacerbation of heart failure (on 2CK Free 120). These conditions cause ATN, not pre-renal. Once again, ↓ flow to the kidney causing pre-renal azotemia will be more subacute/chronic, such as due to NSAID use, recent initiation of diuretic, or dehydration. There are rare Qs that are exceptions, but that is the general principle. - As mentioned earlier, USMLE will give a one-liner where they say, "Dude had surgery where he lost a lot of blood + received many packs of RBCs. 2 days later, he's now recovering in hospital + gets oliguria" (they don't say anything about brown casts) → answer = ATN, not pre-renal. - Likewise, they'll say woman had surgery + had 30-second episode intra-operatively where BP fell to 80/40 → answer = ATN, not pre-renal. - Guy has an MI (cardiogenic shock) + new-onset oliguria → ATN, not pre-renal. - Guy has burns covering 50% of his body + develops oliguria → ATN due to excessive fluid loss → acute ↓ perfusion to kidney. - Acute exacerbation of heart failure causing ATN is a difficult one since heart failure is classically associated with pre-renal from chronic ↓ blood flow to the kidney. But in acute exacerbation of heart failure, we have acute ↓↓ blood flow, leading to ATN (as I said, it's on Free 120).

Other renal conditions associated with ischemia	
Diffuse cortical necrosis	<ul style="list-style-type: none"> - Diffuse cortical necrosis is a term thrown around sometimes and causes confusion for students. I don't think I've ever seen USMLE assess this. I've only seen it show up rarely as an incorrect answer choice. - DCN is simply considered an extension of ischemic ATN, where DCN can occur in severe cases of ischemia (e.g., obstetric hemorrhages). - You can be aware it exists, but don't worry about it for USMLE.
Renal papillary necrosis (RPN)	<ul style="list-style-type: none"> - Renal papillae = parts of kidney where the collecting ducts meet the ureters. - The answer on USMLE for red/dark urine in a patient with sickle cell. - In contrast, if a sickle cell patient has a renal condition + no blood in the urine, the answer = FSGS, as mentioned earlier. - RPN is loss of the renal medulla from ischemia, but unlike ATN, the etiology is usually more subacute or chronic. NSAIDs are a notable cause in this regard, where ↓ afferent blood flow due to ↓ vasodilating prostaglandins over weeks-months causes the medullar blood flow to be slowly choked off. - RPN can occur more acutely in sickle crises, where sickling within microvasculature feeding the medulla results in focal pockets of ischemia. - Pyelonephritis (discussed later) can also cause RPN due to inflammatory compression of the medullar microvasculature. There's one NBME Q I can recall where renal papillary necrosis is the answer due to infection. But I'd say, overall, the highest yield point is just remembering red/dark urine in sickle cell = RPN.

Interstitial nephritis
<ul style="list-style-type: none"> - Exceedingly HY renal condition often confused with ATN. - Aka interstitial nephropathy, or tubulointerstitial nephritis/-nephropathy. - Think of this as "an allergic reaction of the kidney." - 4/5 Qs will be an NSAID, β-lactam, or cephalosporin, followed by getting a maculopapular rash and WBCs (eosinophils) in the urine. This presentation is textbook/pass-level. - Only ~50% of vignettes will mention the maculopapular rash. - The stem need not say "eosinophils" either. They can just say patient is on β-lactam + now has WBCs in the urine + no mention of rash → answer = interstitial nephritis. If they say the rash, it's even easier. - 1/5 Qs will just say a patient was on an NSAID, β-lactam, or cephalosporin and now has mild proteinuria and hematuria. They don't mention a rash or WBCs in the urine. - There is also a singular NBME Q where they just say a patient has simple peripheral edema due to an NSAID, with no mention of anything else, and the answer is interstitial nephropathy. This is more unusual, since "NSAIDs + edema" classically = pre-renal, but I've seen the NBME assess interstitial nephropathy for this as well. - NBME also can give you simple vignette of interstitial nephritis, and then ask for the location in the kidney that's affected (e.g., efferent arterioles, etc.) → answer = "renal tubule." - For example, 40M + treated with nafcillin for 6 weeks for MSSA endocarditis + now has maculopapular rash and eosinophils in the urine; diagnosis? → interstitial nephritis. - 60F + using naproxen (an NSAID) for 6 weeks for her osteoarthritis + has peripheral edema → answer = interstitial nephropathy. - 35F + just recently finished 10-day course of cephalexin + has mild proteinuria and hematuria → answer = interstitial nephropathy. - 35F + taking ibuprofen + has maculopapular rash and eosinophils in the urine; Q asks where in the kidney is fucked up → answer = "renal tubule." Student says, "But don't NSAIDs affect the afferent arteriole?" → Yes, but this particular presentation is clearly tubulointerstitial nephropathy. I haven't seen them be ambiguous here with "NSAID + peripheral edema alone," where you have to debate whether it's interstitial nephropathy or pre-renal. They'll either ask one or the other.

Renal tubular acidosis

Quick notes before discussing RTA:

MUDPILES = mnemonic for high anion-gap metabolic acidoses = **M**ethanol, **U**remia (renal failure), **D**KA, **P**henformin (a drug you don't have to worry about), **I**ron/Isoniazid, **L**actic acidosis, **E**thylene glycol, **S**alicylates (aspirin).

Anion-gap is calculated as $\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$. Normal range is 8-12. High anion-gap = 13 or greater.

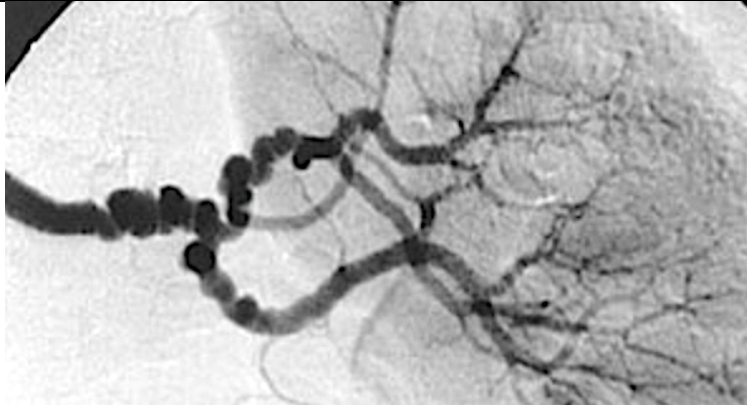
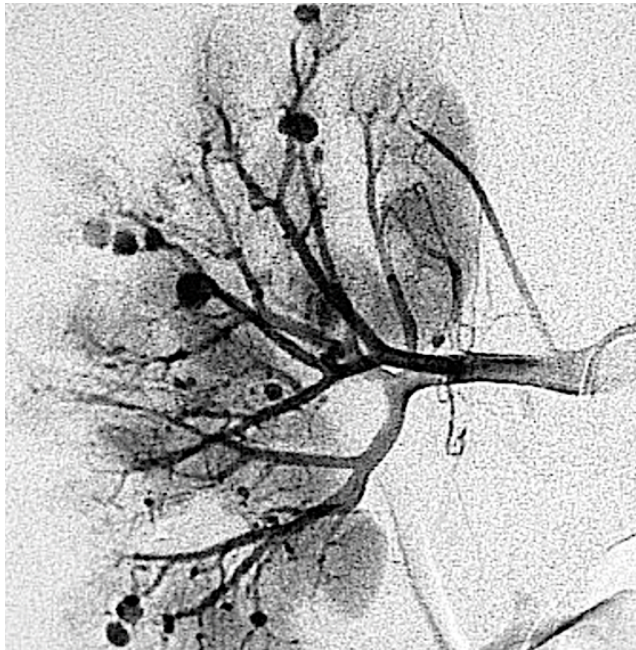
- USMLE really doesn't give a fuck that you know the specifics of types I, II, and IV.
- The way they assess this is by you knowing this is a type of **normal** anion-gap metabolic acidosis (i.e., it is not part of MUDPILES).
- For example, you'll get a 15-line massive paragraph + tons of lab values + have no idea what's going on, but then you calculate the anion gap as 12 (NR 8-12), so you can eliminate all of the MUDPILES answer choices, such as lactic acidosis, DKA, and ethylene glycol poisoning, and you're left with, e.g., Crohn disease or renal tubular acidosis. Then you just say, "Well this clearly ain't Crohn, so it must be RTA." That is how I would say 4/5 RTA Qs show up.
- RTA type I = ↓ ability to secrete H^+ in the cortical collecting duct.
- RTA type II = ↓ ability to reabsorb HCO_3^- in the PCT.
- RTA type IV = renal resistance to aldosterone, or hyporeninemic hypoaldosteronism.
- Type IV presents with hyperkalemia. The others do not. Type III apparently is hyper-rare.
- Type IV will be a patient who has Addisonian-like picture (i.e., ↓ Na^+ , ↑ K^+ , ↓ HCO_3^-), but the vignette will present in a patient who has chronic renal failure.
- Type II can be caused by Fanconi syndrome (discussed more in table below).
- Type I can apparently have renal parenchymal stones (i.e., stones in the actual tissue of the kidney, rather than within the tubular lumina as with traditional nephrolithiasis).
- As I said, the key point is you just know RTA is normal anion-gap / not part of MUDPILES. That'll cover you like 4/5 times.

Other random renal conditions

Tumor lysis syndrome	<ul style="list-style-type: none"> - Lysis of tumor cells (especially leukemic) by chemoradiotherapy leads to release of uric acid and phosphate that can overwhelm the kidneys and cause crystals, namely from uric acid. - USMLE loves asking what can be given to prevent renal failure in patient undergoing chemo → answer = "allopurinol." - Or they'll ask for MOA of drug that can prevent renal failure → answer = "xanthine oxidase." - The arrows USMLE wants for what will be seen in the blood in tumor lysis syndrome is same as renal failure except we also have ↑ uric acid.
Fanconi syndrome	<ul style="list-style-type: none"> - Inability of the PCT to reabsorb "lots of stuff." - Shows up on NBME as an arrow Q, where they ask about the reabsorption of amino acids, glucose, bicarbonate, and phosphate, and the answer is a ↓ for all of them. - Since bicarb reabsorption is impaired, this can lead to RTA type II, but USMLE doesn't really give a fuck. The key point is the ↓ for the reabsorption of the above substrates. - For whatever magical reason, an important cause of Fanconi syndrome is consumption of expired tetracyclines. - Don't confuse Fanconi syndrome with Fanconi anemia. The latter is an autosomal recessive aplastic anemia with hypoplastic thumbs/radii (I've made YouTube clips discussing this).
Hartnup disease	<ul style="list-style-type: none"> - Inability of the PCT to reabsorb tryptophan.

	<ul style="list-style-type: none"> - Can cause niacin (B3) deficiency in theory, since tryptophan is a precursor in niacin synthesis. - This is more just textbook masturbation to be honest that's been parroted over the years. Can't say I've seen this ever assessed once. Just mentioning it here otherwise I'll get some umbrageous student popping into my DMs about it.
Cystinuria	<ul style="list-style-type: none"> - Cystine stones (hexagonal) can occur in young adult due to an inability to reabsorb the COLA (dibasic) amino acids → Cysteine, Ornithine, Lysine, Arginine. - Cystine is two cysteines put together. - Cystinuria can be diagnosed with cyanide-nitroprusside test.
Hepatorenal syndrome	<ul style="list-style-type: none"> - Nonsense diagnosis on USMLE that will sometimes show up as an incorrect / distractor answer choice. - Apparently liver failure can sometimes cause renal failure via obscure mechanisms. - Renal biopsy will be normal almost always.
Thin glomerular basement membrane disease	<ul style="list-style-type: none"> - Benign familial condition where patient can have mild hematuria. - Thin basement membranes allow for passage of small amounts of RBCs. - No treatment necessary.

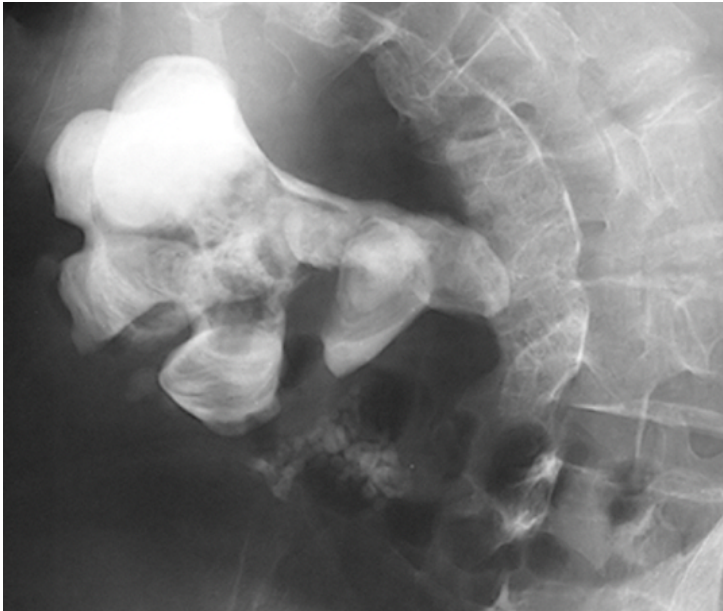
Renovascular hypertension	
Renal artery stenosis (RAS)	<ul style="list-style-type: none"> - Narrowing of one or both renal arteries due to atherosclerosis that causes ↑ renin-angiotensin-aldosterone system (RAAS) and ↑ BP. - Q will be patient over the age of 50 with cardiovascular disease risk factors, such as diabetes, HTN, and/or smoking. - Patients who have pre-existing HTN causing atherosclerosis leading to RAS will often have 10-20 years of background HTN that then <i>becomes accelerated</i> over a few-month to 2-year period. What this means is: the slowly developing atherosclerosis in the renal arteries finally reaches a point at which the kidney is unable to maintain autoregulation, and the RAS is now clinical (i.e., accelerated HTN of ↑↑ BP within, e.g., 3 months). - Another way USMLE will give RAS is by giving ↑ BP in patient with significant evidence of atherosclerotic disease (i.e., Hx of coronary artery bypass grafting, intermittent claudication), and then ask for the most likely cause → RAS. You have to say, "Well he clearly has atherosclerosis in his coronaries and aortoiliac vessels, so that means he'll have it in the renal arteries too." - Q can say older patient with carotid bruit has recent ↑↑ in BP and then ask for diagnosis → answer = RAS. Similar to above, if the patient has atherosclerosis in one location (i.e., the carotids), then he/she will have it elsewhere too. - HY factoid about RAS is that ACEi or ARBs will cause renin and/or creatinine to go up. This is a HY point that is often overlooked and is asked on NBMEs. I have not seen NBME care whether it's uni- or bilateral in this case. → Kidney can autoregulate across flux in perfusion. Patients with already-compromised renal blood flow are more sensitive to the subtle ↓ in filtration fraction that occurs secondary to ACEi/ARB use, so renin/creatinine ↑. - If USMLE gives you unilateral RAS, renin is only ↑ from that kidney. The other kidney will not produce ↑ renin. - After renin and aldosterone levels are obtained, MR angiography of the renal vessels is what USMLE wants for the next best step in diagnosis.
Fibromuscular dysplasia (FMD)	<ul style="list-style-type: none"> - The answer on USMLE for narrowing of the renal arteries in a woman 20s-40s. - Not the same as renal artery stenosis, and not caused by atherosclerosis. - If you broadly say "renal artery stenosis," that specifically refers to atherosclerosis of the renal arteries in patient >50 with CVD. - FMD is tunica media hyperplasia (not dysplasia, despite the name) that results in a "string of beads" appearance on renal angiogram.

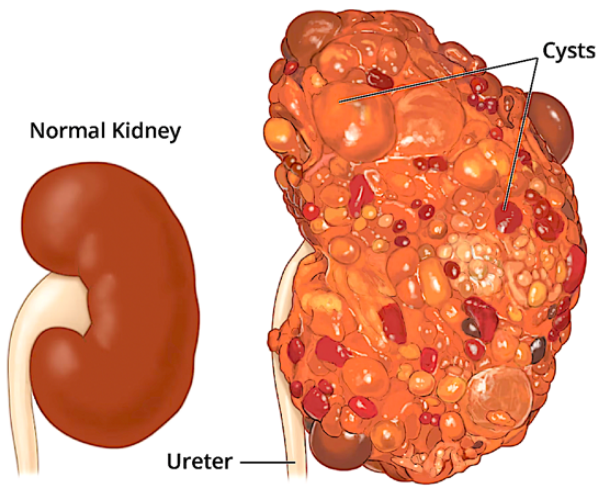
	 <ul style="list-style-type: none"> - MR angiography is answer on NBME for diagnostic modality. - Can affect the carotid vessels. A 2CK Surg Q gives FMD vignette and also says there is 25% occlusion of one of the carotids.
Polyarteritis nodosa (PAN)	<ul style="list-style-type: none"> - As discussed in the cardio PDF, this is a medium-vessel vasculitis that causes a “string of pearls” appearance of the renal vessels. This can be confused with FMD, but note the difference in the imaging. FMD shows more beading along the larger/proximal arterial sections, whereas PAN shows pearls more at the vascular termini, with the more proximal parts more likely to be spared.  <p>Angiogram of PAN shows pearls that are more distal in the renal vasculature; FMD, in contrast, shows more proximal beading, with the termini not as conspicuously involved.</p> <ul style="list-style-type: none"> - There is an NBME Q where they list both PAN and FMD as answer choices and it relies on you knowing the angiogram to get it right. They don't mention hepatitis B, but answer is PAN. That's why I'm harping on this here. - Causes fibrinoid necrosis. - Can be caused by hepatitis B. - Spares the pulmonary vasculature.
Renal artery thrombosis	<ul style="list-style-type: none"> - The answer on USMLE for hypertension in a neonate following umbilical artery catheterization. USMLE simply wants “↑ renin, ↑ aldosterone” as the answer.

	<ul style="list-style-type: none"> - Sounds weird, but you need to know umbilical artery catheterization is a major risk factor for renal artery thrombosis in neonates. - 2CK NBME Q gives brief umbilical artery catheter insertion in kid born 26 weeks' gestation in order to monitor blood pressure for a pneumonia. 3 weeks later, he has \uparrow BP (128/86) \rightarrow answer = "\uparrow renin, \uparrow aldosterone" as answer. - BP in term neonates should be \sim60/40. In a preemie 29 weeks' gestation, it should be \sim50/30 according to Google.
--	---

HY Uremia points	
<ul style="list-style-type: none"> - As mentioned earlier, "uremia" means "urea in the blood," but is used to refer to patients who have symptomatic renal failure with poor lab values. - On USMLE, uremic patients will have: \uparrow K^+, \downarrow HCO_3^-, \downarrow Ca^{2+}, \uparrow PO_4^{3-}. Na^+ is variable. 	
Uremic pericarditis	<ul style="list-style-type: none"> - Friction rub in patient with \uparrow BUN and Cr. - Answer = hemodialysis.
Uremic encephalopathy	<ul style="list-style-type: none"> - Mental status change in patient with \uparrow BUN and Cr. - Answer = hemodialysis.
Uremic platelet dysfunction	<ul style="list-style-type: none"> - Nosebleeds and/or petechiae in patient with renal failure. - Qualitative, not quantitative, platelet problem. In other words, bleeding time is \uparrow, but platelet count is normal. - Mechanism is \uparrow BUN causing impairment of platelet function. - Answer on USMLE can be written as "acquired platelet dysfunction." - Treatment = hemodialysis. - On 2CK NBME 10, Surg Q wants "initiation of dialysis" as answer in uremic patient pre-op. Improving RFTs will \downarrow peri-op morbidity/mortality + \downarrow risk of intra-op bleeding due to uremic platelet dysfunction.
Uremic frost	<ul style="list-style-type: none"> - Yellow skin sometimes seen in severe renal failure due to \downarrow ability to excrete urea. Excess is excreted in sweat, precipitating out as white crystalline deposits (frost). - Can be associated with itchy skin (uremic pruritis).

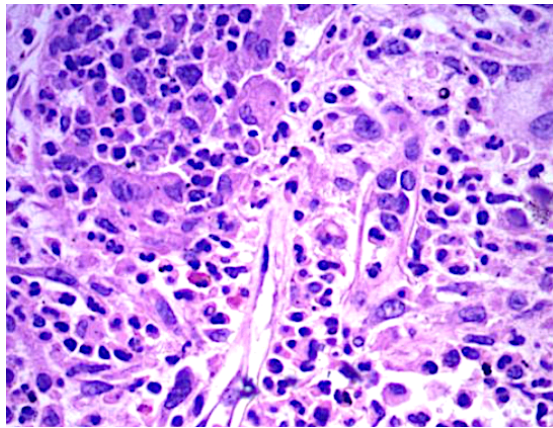
Urolithiasis	
<ul style="list-style-type: none"> - Urolithiasis is broad, umbrella term that refers to both nephrolithiasis and ureterolithiasis. - Diagnosed with non-contrast CT of abdomen and pelvis. - KUB (X-ray of kidney, ureters, bladder) can be done but isn't as sensitive (although below I show an X-ray). 	
Stone type	HY points
Calcium	<ul style="list-style-type: none"> - Most common type of stone. Can be calcium oxalate or calcium phosphate, although I've never seen USMLE once assess or give a fuck about phosphate stones. - Most young adults with idiopathic kidney stones will have "normocalcemia and hypercalciuria" – i.e., normal serum calcium but elevated urinary calcium. - USMLE will give you healthy male in his 20s with sharp pain in the flank or groin + RBCs in the urine \rightarrow answer = urolithiasis. - Crohn disease and disorders causing fat malabsorption increase the risk for calcium oxalate stones (\uparrow fat retained in GI tract \rightarrow \uparrow chelation with calcium in GI tract \rightarrow \downarrow calcium available to bind oxalate \rightarrow \uparrow oxalate absorption by GI tract \rightarrow \uparrow urinary oxalate). - Primary hyperparathyroidism and malignancy causing hypercalcemia are HY etiologies. - Milk-alkali syndrome: \uparrow calcium + \uparrow bicarb + calcium stones. Textbook scenario is a patient taking too many antacids, but vignette will usually not mention this and it will simply be a diagnosis of exclusion (i.e., you eliminate to get there). - Ethylene glycol (Anti-Freeze) and hypervitaminosis C can cause oxalate stones. - First step in prevention and treatment of stones is "adequate hydration." - Thiazides can be used to prevent recurrent stones by \downarrow urinary calcium. NBME has a Q that asks why \rightarrow answer = \uparrow reabsorption of calcium.

	<ul style="list-style-type: none"> - In theory, alkalization of the urine can help treat oxalate stones, and acidification of the urine can help treat phosphate stones.
Struvite	<ul style="list-style-type: none"> - Composed of ammonium magnesium phosphate. - Formed in \uparrow pH in the presence of urease (+) bacteria. - <i>Klebsiella</i>, <i>Serratia</i>, and <i>Proteus</i> are HY causes. - These stones are large, ram-horn like. The image is HY.  <ul style="list-style-type: none"> - Apart from adequate hydration, Tx is acidification of urine with NH_4Cl + surgery.
Uric acid	<ul style="list-style-type: none"> - Seen in patients who have gout. Not complicated. - First-line Tx for <i>chronic</i> gout is xanthine oxidase inhibitors (i.e., allopurinol or febuxostat). They are preferred over uricosurics (meaning \uparrow urinary excretion of uric acid) like probenecid and sulfinpyrazone because the latter agents \uparrow risk of uric acid stones. - Probenecid and sulfinpyrazone inhibit organic anion transporter (OAT), which normally functions to \uparrow absorption of uric acid. - Weird factoid about probenecid is that it can help maintain serum β-lactam levels, since the latter are excreted by OAT. There's an NBME Q around somewhere that asks about this. Sometimes old-school docs will put a patient on a β-lactam and probenecid. Don't be confused by this. The patient doesn't have gout. It's just a way of \downarrow renal excretion of the β-lactam.
Cystine	<ul style="list-style-type: none"> - As mentioned earlier, cystine is two cysteines put together. - Cystine stones (hexagonal) can occur in young adult due to an inability to reabsorb the COLA (dibasic) amino acids \rightarrow Cysteine, Ornithine, Lysine, Arginine. - Cystinuria can be diagnosed with cyanide-nitroprusside test.
Miscellaneous	<ul style="list-style-type: none"> - Acyclovir (for HSV and shingles) and indinavir (for HIV) can cause crystal nephropathy. Not particularly HY, but worthy of 1-2 lines here.

Cystic kidneys	
ADPKD	<ul style="list-style-type: none"> - Autosomal dominant polycystic kidney disease; chromosome 16. - The answer on USMLE if disease starts as an adult (i.e., 30s-40s). - Cysts are technically present early in life, but only become clinical as adult (i.e., \uparrow BP and \uparrow RFTs). <p style="text-align: center;">Polycystic Kidney</p>  <ul style="list-style-type: none"> - These patients have \uparrow BP due to \uparrow RAAS (compression of microvasculature of kidney due to enlarging cysts). - Can cause saccular (berry) aneurysms of the circle of Willis \rightarrow risk for subarachnoid hemorrhage. - Highest yield point is that serial blood pressure checks are correct over circle of Willis MR angiogram screening. Latter is wrong answer on USMLE. MR angiogram screening of circle of Willis is only done when there is (+) family Hx of SAH or saccular aneurysms. - NBME gives easy vignette of ADPKD, and then the answer is just "polycystin" as the protein that's fucked up. Sounds obvious, but it's asked so I'm mentioning it. - Cystic kidneys are part of "ciliopathies," which is obscure term that refers to conditions where cilia are abnormal. Polycystin is a protein required for cilia function on renal epithelium. - Most common extra-renal location for cysts is the liver (85% by age 30).
ARPKD	<ul style="list-style-type: none"> - Autosomal recessive polycystic kidney disease; chromosome 6. - The answer on USMLE for cystic kidneys in pediatrics. - Can be associated with hepatic fibrosis.
Miscellaneous	<ul style="list-style-type: none"> - Just be aware renal cysts can occasionally develop in other conditions, such as chronic dialysis patients. - Conditions such as medullary sponge kidney are garbage for USMLE. Waste of time.

HY anatomic abnormalities	
Posterior urethral valves (PUV)	<ul style="list-style-type: none"> - Most common genitourinary abnormality in neonatal males. - Urethra has abnormal presence of valves at the posterior (prostatic) urethra, preventing the outflow of urine. - USMLE will give Qs of varying severity. - Most severe is <i>in utero</i> oligohydramnios. - Can present as 12-hour-old neonate who hasn't yet urinated + has suprapubic mass (i.e., full bladder). - Can also present as 6-week-old boy who has full bladder (i.e., possibly slower accumulation due to only partially obstructed outflow). - Obstructed outflow \uparrow risk for UTIs, cystitis, and pyelonephritis.

	<ul style="list-style-type: none"> - Apart from knowing this diagnosis, highest yield point is that we do ultrasound followed by voiding cystourethrogram to diagnose. - NBME Qs might already mention negative ultrasound in the vignette, or might omit it altogether, where you just select "voiding cystourethrogram."
Vesicoureteral reflux	<ul style="list-style-type: none"> - Congenital abnormality in which urine from the bladder can go back up into the ureter toward the kidney. - This ↑↑ risk for recurrent acute pyelonephritis → chronic pyelonephritis (as I discuss below). - Can also occur in pregnancy due to 2 reasons: 1) larger uterus in 3rd trimester can compress the ureters; 2) progesterone ↓ ureteral peristalsis. - This is why pregnant women can get pyelonephritis, and also why we always treat asymptomatic bacteriuria in pregnancy, whereas we don't treat it if woman is not pregnant.
Ureteral atresia	<ul style="list-style-type: none"> - Bit of a weird one, but not me being fancy. It's on NBME. - "Failure of canalization of proximal ureter" will be the answer if they tell you the renal collecting duct system is dilated, but the ureters are not dilated. - Sounds obvious, but I see students get this wrong a lot. - You need to simply know: kidneys → ureters → bladder → urethra, and if we have a congenital obstruction at any point, that could be referred to as "failure of canalization." - "Congenital ureteral obstruction" is an answer on one of the NBMEs for chronic pyelonephritis causing tubular atrophy (once again, discussed below).

Genitourinary infection-related stuff	
- For all of the STD/STI-related stuff, I cover that in the Repro/Obyn section. I'm keeping this small table more limited to kidney/bladder stuff.	
Acute pyelonephritis	<ul style="list-style-type: none"> - Infection of the kidney. "Pyelo" means kidney. - 9/10 questions will mention fever + costovertebral angle (CVA) tenderness, which is pain with percussion of the flank. - "Granular casts" can be seen. Do not confuse this with acute tubular necrosis. "General granular casts" can sometimes be seen in pyelonephritis and dehydration. It's on one of the 2CK IM forms, where students say, "Wait, but they say granular casts; how is this not ATN?" - Major risk factors are vesicoureteral reflux (especially in pregnancy) and posterior urethral valves. - Most common organism is <i>E. coli</i>. Other organisms, i.e., <i>Klebsiella</i>, <i>Serratia</i>, and <i>Proteus</i> cause struvite stones. - Neutrophilic infiltration will show up as lots of blue/purple (basophilic) cells on histo. USMLE likes this image. 

	<ul style="list-style-type: none"> - For above image, you say, "Mike I feel weird. Idk what I'm looking at." The blue cells are neutrophils infiltrating the kidney in acute pyelo. The USMLE will show images basically identical to this for a variety of infections, e.g., prostatitis, where the bigger picture concept is, "Oh that's acute inflammation. Those purple cells are neutrophils." <i>That's</i> what USMLE wants you to know. For instance, a nearly identical image of prostate histo in old dude with prostate pain and fever → you'd know immediately it's prostatitis. - It's to my observation bacteria can be few in the urine in acute pyelo. This confuses some students. But it's typically what I see on NBME forms. If the infection is further down, i.e., UTI in the urethra, then bacteria are more copious. - Treatment for pyelo is ciprofloxacin or ceftriaxone. USMLE is known to ask these. - Persistent fever despite Abx Tx → do CT to look for perinephric abscess. - For example, old dude + high Cr (caused by post-renal from BPH) + treated for pyelo → now gets sore ankle → was treated with cipro (causes tendonopathy). - 2CK form has ceftriaxone as an answer in pyelo Q where cipro isn't listed. But cipro is classic Tx. It's to my observation that ceftriaxone is HY drug on 2CK for community-acquired "general sepsis" or "general complicated/severe infections" – i.e., it is hard-hitting and covers wide array of community organisms. - There is one 2CK Q where they mention pyelo is treated with amp + gent in the stem, but I've never seen this assessed as an answer you need to choose. I've only ever seen ciprofloxacin or ceftriaxone as actual NBME answers for pyelo.
Chronic pyelonephritis	<ul style="list-style-type: none"> - Due to recurrent acute pyelonephritis. - Almost always pediatric, where they give a 4-year-old who has a small, shrunken kidney with tubular atrophy and blunting and scarring of the renal calyces. <div data-bbox="667 1037 1209 1630" data-label="Image"> </div> <p>Kidney appears to show loss of architecture + scarring.</p> <ul style="list-style-type: none"> - USMLE will show you kidney that looks similar to the above in a child with recurrent UTIs, and then the answer is just "tubular atrophy" for what is most likely to be seen on microscopic examination. - Another Q shows the same image and the answer is "congenital ureteral obstruction" as the cause. - "Thyroidization of the kidney" is a buzzy phrase that has been applied to chronic pyelo over the years, but USMLE doesn't so much care about this. What they really like is the tubular atrophy and scarring / loss of architecture of the calyces. - Chronic pyelo doesn't present with cellular infiltration the way acute pyelo does. It refers to the kidney being destroyed/shrunken from repeated prior infections.

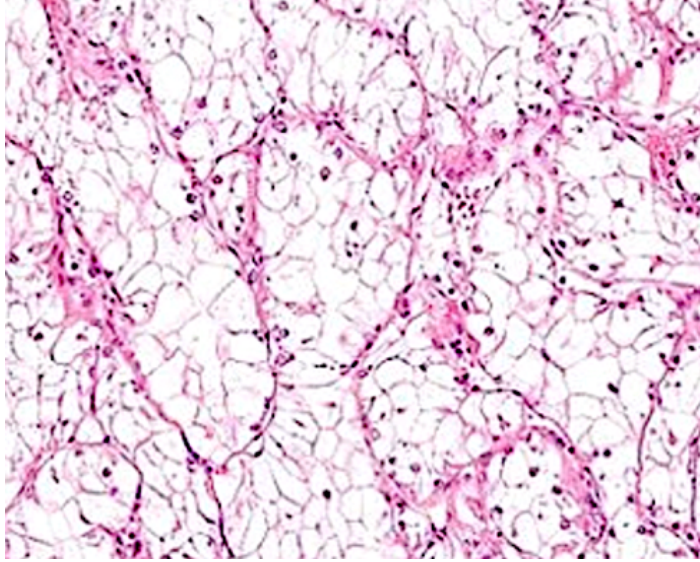
Cystitis	<ul style="list-style-type: none"> - Suprapubic tenderness in female. Patient need not have fever. - <i>E. coli</i> most common cause. HY for USMLE you know fimbriae and pilus proteins facilitate <i>E. coli</i>'s attachment to urothelium. - Will have bacteria and WBCs in the urine (i.e., bacteriuria + pyuria). - Urinary nitrites and leukocyte esterase can be positive. These just reflect bacterial infections. Some students get pedantic about which organisms result in which combo of (+) or (-) findings here, but that's low-yield for USMLE. - Can be caused by suprapubic catheters (on 2CK IM and Surg). - Nitrofurantoin is HY drug to treat cystitis on USMLE.
Chronic interstitial cystitis	<ul style="list-style-type: none"> - Not an infection. - This is >6 weeks of suprapubic tenderness + dysuria (pain with urination) that is unexplained, where laboratory and urinary findings are negative. - They can mention anterior vaginal wall pain (bladder is anterior to vagina). - USMLE wants you to know you don't treat. Steroids are wrong answer. "Treatment" is standard placating placebo nonsense such as "education," "self-care" and "physiotherapy."
General UTI	<ul style="list-style-type: none"> - Classically <i>E. coli</i> infection of the urethra. - Common in women due to shorter urethras. - As mentioned above for cystitis, fimbriae and pilus proteins facilitate <i>E. coli</i>'s attachment to urothelium. - Inoculation of the urethra following sexual activity is most common mechanism. - Can be caused by catheters. You need to know dysuria + Hx of catheter = UTI. - Tangentially, this is also HY for general sepsis, where if they mention Hx of IV line/catheter, USMLE wants you to be able to say, "Got it. That's the cause." - Trimethoprim, trimethoprim/sulfamethoxazole (TMP/SMX), or nitrofurantoin are standard treatments for UTI. - For prevention, post-coital voiding confers ↓ risk of recurrence. - If post-coital voiding doesn't work, "post-coital nitrofurantoin therapy" is answer on 2CK NBME form. - If post-coital nitrofurantoin therapy doesn't work, "daily TMP/SMX prophylaxis" is the answer. Sounds absurdly wrong / like a bad idea, but it's an answer a couple times on 2CK assessments. - There's also a Q where they say a girl was treated successfully in the past with TMP/SMX for a UTI + ask how to prevent recurrent UTIs now, and they just jump straight to "daily TMP/SMX prophylaxis." - If patient is treated for a UTI and dysuria persists, the next best step is testing for <i>Chlamydia</i> and <i>Gonorrhea</i>.

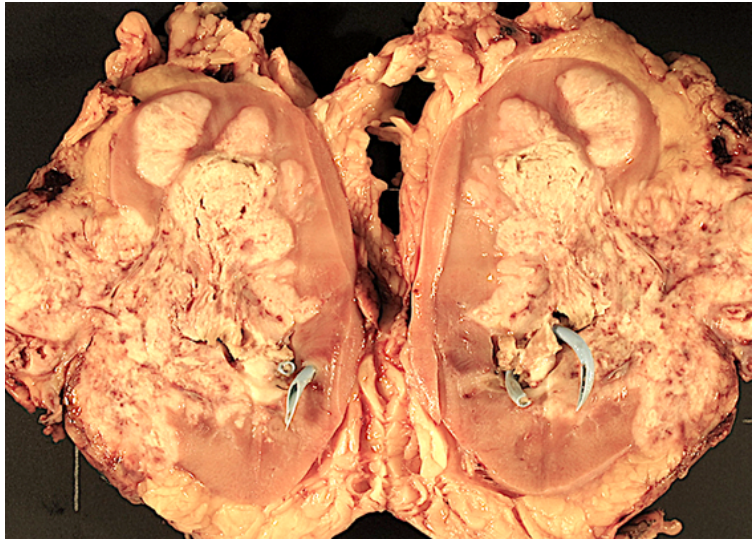
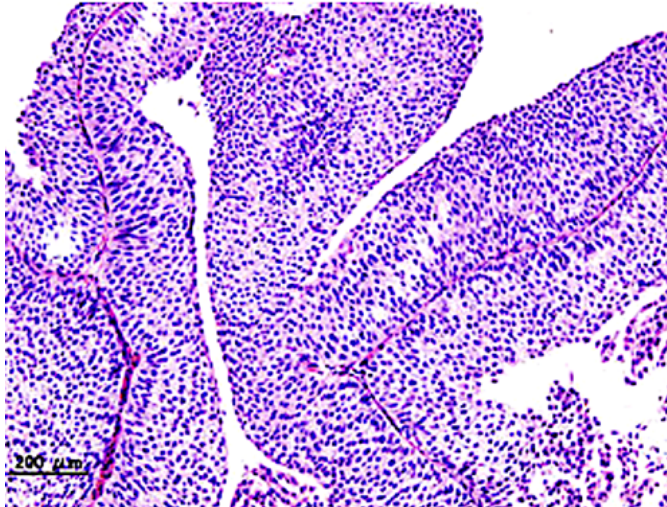
HY Bladder incontinences	
Stress	<ul style="list-style-type: none"> - The answer for loss of urine with ↑ intra-abdominal pressure from laughing, sneezing, coughing. - Stereotypical risk factor is grand multiparity (i.e., Hx of many childbirths) leading to weakened pelvic floor muscles. - I'd say only ~50% of Qs will mention Hx of pregnancy. The other ~50% are idiopathic. - Buzzy vignette descriptors and answer choices are: "downward mobility of the vesicourethral junction," "urethral hypermobility," and "urethral atrophy with loss of urethrovesical angle." - Treatment is pelvic floor (Kegel) exercises. These notably strengthen levator ani, pubococcygeus, and the external urethral sphincter. - USMLE is known to ask which muscle is <i>not</i> strengthened by Kegel exercises, which sounds obscure, since any muscle could theoretically be the answer ("Well the deltoid isn't strengthened."). But a favorite answer here is internal urethral sphincter. The way you know this is the answer is because internal sphincters are under sympathetic (i.e., involuntary; autonomic) control, which means it's impossible to strengthen it via a

	<p>voluntary (i.e., somatic) exercise. USMLE doesn't expect you to be an obstetrician. The bigger picture concept is simply knowing internal sphincter control is involuntary. It is external sphincter control that is voluntary (somatic).</p> <ul style="list-style-type: none"> - Do not give medications for stress incontinence on USMLE. - If Kegel exercises fail, patients can get a mid-urethral sling (LY; asked once).
Urge	<ul style="list-style-type: none"> - The answer on USMLE for patient who has an "urge" (NBME will literally say that word and I've seen students get the Q wrong) to void 6-12+ times daily unrelated to sneezing, coughing, laughing, etc. (otherwise stress incontinence). - Ultra-HY for multiple sclerosis. I've had students ask whether MS is urge or overflow. It shows up repeatedly on the NBMEs as urge; I've never seen it associated with overflow. I'd say ~1/3 of urge incontinence vignettes on NBME forms are MS. - Other vignettes will be peri-menopausal women, or idiopathic in old women. - Mechanism is "detrusor hyperactivity," or "detrusor instability." - Vignette can mention woman has urge to void when stepping out of her car, or when sticking her key in the car/front door of her house. Sounds weird, but these are important Qs to ask when attempting to diagnose urge incontinence. - UTIs can present similarly to urge incontinence. Some students have asked, "Well isn't that because UTIs are a cause of urge incontinence?" Not really. It just happens to be that UTIs can sometimes cause transient urinary urgency. For example, if they give a Q where they say patient had Hx of urinary catheter + now has dysuria and urinary urgency, answer = "urinary tract infection" on NBME; "detrusor hyperactivity" is wrong answer. - Treatment is oxybutynin (muscarinic receptor antagonist); this ↓ activity of the detrusor muscle of the bladder. - Some students get hysterical about mirabegron (β3-agonist), but I've never seen NBME forms assess this.
Overflow	<ul style="list-style-type: none"> - Will be due to either BPH or diabetes on USMLE. - Will have ↑ post-void volume. Normal is < ~50 mL. On USMLE for overflow, they'll give you 300-400 mL as post-void volume. - As I talked about earlier for BPH, they will give old dude + high creatinine (post-renal azotemia). Next best step is "insertion of catheter" to relieve the obstruction. If they don't have this listed, "measurement of post-void volume" can be an answer. We then treat the BPH with finasteride (5α-reductase inhibitor) or an α1-blocker (tamsulosin, terazosin). - For diabetes, the mechanism is neuropathy to the bladder causing "neurogenic bladder," or "hypotonic bladder," or "hypocontractile bladder/detrusor muscle." - For neurogenic bladder causing overflow incontinence + ↑ post-void volume, remember that USMLE is first obsessed with "measure post-void volume" and "insertion of catheter" if they are listed. They will not force you to choose between the two. But they like these answers prior to giving medications. - Give bethanechol (muscarinic receptor agonist); this stimulates the detrusor muscle. - Making sure you don't confuse oxybutynin and bethanechol is pass-level for USMLE.
Normal pressure hydrocephalus (NPH)	<ul style="list-style-type: none"> - Patient who has "wet, wobbly, wacky" presentation (i.e., urinary incontinence, ataxia, cognitive changes) +/- Parkinsonism (e.g., short-steppage gait). - Caused by failure of reabsorption of CSF by the arachnoid granulations, resulting in impingement on the zona radiata and "failure to inhibit the voiding reflex" (answer on NBME). - Enlargement of the lateral ventricles on head CT.
AIDS complex dementia	<ul style="list-style-type: none"> - Presents similar to NPH – i.e., "wet, wobbly, wacky" in AIDS patient.

Urinary retention diagnoses	
Bladder neck dyssynergia	<ul style="list-style-type: none"> - Lack of coordination between bladder sphincters and detrusor muscle. - HY cause is spinal cord injury, which can cause either inability to void or urinary incontinence. - MS is another theoretical cause, which is where “overflow incontinence” as a result of MS has been asked by students, but once again, I’ve only ever seen urge incontinence for MS on NBME exams. Qbank ≠ NBMEs.
Bladder outflow obstruction	<ul style="list-style-type: none"> - Acute urethral obstruction due to catheter removal is HY on 2CK forms. - They’ll say patient has <i>anuria</i> (i.e., no urinary output at all) following removal of a catheter. - “Acute urethral obstruction” or “bladder outflow obstruction” is the answer. - Treatment on NBME is “re-insertion of urinary catheter.”
Cauda equina syndrome	<ul style="list-style-type: none"> - Will present as leg pain + urinary retention on USMLE. - Can be idiopathic, from disc herniation, or other trauma. - Metastases is HY cause (i.e., random guy over 50; or female with Hx of mastectomy 5 years ago). - “Saddle anesthesia” is an overrated detail and doesn’t show up in the vast majority of NBME Qs, as per my observation. - Cauda equina is the collection of nerves at the end of the spinal cord. Impingement on these nerves is what causes the syndrome. I cover this stuff in more detail in my HY Neuroanatomy PDF.

HY Genitourinary injuries	
Urethral injury	<ul style="list-style-type: none"> - Always presents with blood at the urethral meatus. - 3 ways this presents on USMLE: <ol style="list-style-type: none"> 1) Blood at urethral meatus + saddle injury (dude falls on balance beam). 2) Blood at urethral meatus + pelvic fracture/instability. 3) Blood at urethral meatus + “prostate not palpable.” - Next best step is retrograde urethrogram.
Bladder injury	<ul style="list-style-type: none"> - Answer on USMLE for blunt force trauma to abdomen + exquisite suprapubic tenderness + catheter insertion yields 10-30 mL of dark bloody fluid. - Next best step is retrograde cystourethrogram. Do not confuse with voiding cystourethrogram, which is for posterior urethral valves.
Ureteral injury	<ul style="list-style-type: none"> - Just be aware this is USMLE-favorite injury for any surgery done in the gynecologic area. - Diagnosis is with retrograde pyelogram or CT urogram, although I haven’t seen the USMLE give a fuck. Any ureter injury Q I’ve seen just has “ureter” as answer.
Renal injury	<ul style="list-style-type: none"> - Exceedingly HY on 2CK. - Will present as bruising or pain over a flank following accident. - Blood in the urine is highly sensitive, meaning if it’s not there, we can rule-out. - First step in diagnosis: “Is there gross blood in the urine?” If yes → do CT of the abdomen with contrast to diagnose (sounds wrong, since we’re worried about kidney injury, so student says, “Why would we use contrast?” But it’s what USMLE wants. Ultrasound is wrong answer). - If patient does not have gross blood in the urine, next best step is urinalysis looking for microscopic blood. If present → answer = CT of the abdomen with contrast. If negative → “no further diagnostic studies indicated.”

Urothelial malignancies	
Renal cell carcinoma (RCC)	<ul style="list-style-type: none"> - Aka "clear cell carcinoma"; this is most common variant of RCC. - Classic Q is a smoker over 50 with red urine and a painful flank mass. - Q need not mention smoking, but it is biggest risk factor. - USMLE likes the histo for this, which will show you large clear cells.  <ul style="list-style-type: none"> - Can cause polycythemia due to ↑ EPO and hypercalcemia due to PTHrp secretion (correct, same as squamous cell carcinoma of the lung). - For example, they say 55-year-old male + red urine + polycythemia + hypercalcemia + show you above image; they ask for the source of the malignancy → answer "kidney," not lung. Squamous cell carcinoma of the lung won't cause hematuria, nor does it metastasize to the kidney.
Wilms tumor (Nephroblastoma)	<ul style="list-style-type: none"> - The answer for painless flank mass in a kid age 2-4 years. - Does not present in newborns. If they give you a 12-hour-old male, for instance, with a midline mass, that is posterior urethral valves causing a full bladder (let alone the fact they say "midline," not flank). I've seen tons of students select Wilms for this, and I'm like, is the kidney in your midline? - If they give you a kid 2-4 years with a midline mass, that is neuroblastoma. - For whatever magical reason, you need to know Wilms tumor is sometimes caused by mutations on chromosome 11. They ask this factoid on 2CK as well. There are various Wilms tumor syndromes you need to be aware of: <ul style="list-style-type: none"> - Beckwith-Wiedemann syndrome <ul style="list-style-type: none"> - Wilms tumor + macrosomia (big baby >4,000g) + hemi-hypertrophy (half of the body is bigger than the other) + macroglossia + omphalocele + hypoglycemia. - Hard 2CK Q gives newborn with macrosomia + hemi-hypertrophy + macroglossia + omphalocele; they don't mention a Wilms tumor (makes sense, since we said we won't see it in newborns); they ask for what else could be seen in this patient → answer = "hypoglycemia." I say hard Q because Wilms plays no role in the vignette. - WAGR syndrome <ul style="list-style-type: none"> - Wilms tumor, Aniridia (iris abnormalities), Genitourinary anomalies, Retardation. - Usually an easy Q, where they mention "aniridia" straight up in the vignette and then the answer is just "Wilms tumor" for what the kid can go on to develop.

	<ul style="list-style-type: none"> - Denys-Drash syndrome <ul style="list-style-type: none"> - Ambiguous genitalia + Wilms tumor.
Collecting duct carcinoma	<ul style="list-style-type: none"> - Rare as fuck. 0-3% of renal malignancies. But shows up on NBME.  <ul style="list-style-type: none"> - Offline NBME Q shows some pic of a kidney split open like this and then the answer is just "naphthylamine" (moth balls) as the causative agent.
Transitional cell carcinoma of the bladder	<ul style="list-style-type: none"> - Most common bladder cancer. - Classic vignette is hematuria in smoker <i>without</i> a painful flank mass or polycythemia/hypercalcemia (otherwise RCC). - USMLE wants you to know smoking is most common risk factor, but aniline dyes (industrial clothing dyes) and naphthylamine are important causes. - 2CK Surg Q gives Stage 0 bladder cancer vignette; answer is just "endoscopic resection." - I've never seen BCG vaccine as correct answer on NBME. I've only seen it as a distractor. For whatever reason, some studies in the past have suggested intra-cystic instillation of the TB vaccine can help with bladder cancer. But this is wrong on USMLE.  <p>Can have papillary structure on histo.</p>
Squamous cell carcinoma of the bladder	<ul style="list-style-type: none"> - Can be caused by <i>Schistosoma hematobium</i> (a trematode or fluke, which is a type of helminth). - <i>S. hematobium</i> lays its eggs in the bladder wall and cystic veins draining the bladder.

	- Vignette will be young guy who has red urine months after returning from Africa where he went swimming in a lake → answer is just <i>Schistosomiasis</i> . Or they ask what he's at ↑ risk of → answer = squamous cell carcinoma.
--	---

Obscure miscellaneous conditions	
Bartter syndrome	- Disease that presents as though patient is on loop diuretic. - For whatever magical reason, is associated with juxtaglomerular cell hyperplasia.
Gitelman syndrome	- Disease that presents as though patient is on thiazide diuretic.




Hyper-terse summary of drugs causing HY renal conditions	
- Discussed all this stuff earlier. But students confuse this stuff a lot. So the summary is warranted.	
Acute tubular necrosis	- Aminoglycosides (gentamicin, tobramycin, amikacin). - Cisplatin.
Interstitial nephritis	- NSAIDs, β -lactams, cephalosporins.
Membranous glomerulonephropathy	- Dapsone, gold salts, sulfonamides.


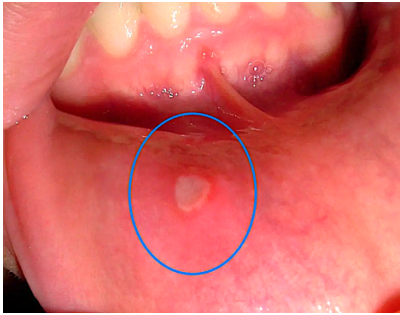


Diuretics / Renal-related drugs	
Mannitol	- Osmotic diuretic that ↑ osmolality of urine, thereby retaining free water within the PCT and descending limb of loop of Henle. - Can be used as Tx for ↑ intracranial pressure after patient has been intubated + hyperventilated (\downarrow CO ₂ → \downarrow cerebral perfusion). - Avoid in heart failure (transient ↑ in serum osmolality prior to renal excretion → ↑ retention of free water within vascular space → transient ↑ preload on heart).
Acetazolamide	- Carbonic anhydrase inhibitor (enzyme that enables $\text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+$) that acts within the tubular cells of the PCT. - Classic use is altitude sickness → causes \downarrow reabsorption of HCO_3^- in the PCT → results in ↑ urinary pH and volume + \downarrow serum pH and volume. In altitude sickness, patients hyperventilate (\downarrow CO ₂ → ↑ pH) to take in more O ₂ , but it takes a minimum of 12-24 hours for the kidney to \downarrow HCO_3^- reabsorption, so acetazolamide forces the \downarrow reabsorption by causing metabolic acidosis.
Expired tetracyclines	- Can cause Fanconi syndrome (\downarrow ability of PCT to reabsorb amino acids, glucose, bicarb, and phosphate).
Furosemide	- Classic loop diuretic that inhibits the apical $\text{Na}^+/\text{K}^+/\text{2Cl}^-$ ATPase symporter on the thick ascending limb. Apical means side of urine. Basolateral means side of blood.




	<ul style="list-style-type: none"> - Most efficacious diuretic at enabling fluid unloading for pulmonary and peripheral edema. - Answer on USMLE for patient with heart failure who has ↓ O₂ sats who “refuses to lie supine/back on the gurney” because he/she can’t breathe. Q might say CXR or exam shows fluid 2/3 up the lung fields. - Also answer for first drug to ↓ peripheral edema. - Application of loops can be confused by students with ACEi/ARB. For instance, the latter are used first-line to ↑ EF in heart failure even if O₂ sats are low (↓ AT-II constrictive effect on arterioles → ↓ afterload → heart pumps easier), but loops are first-line if the vignette <i>specifically emphasizes</i> the dyspnea and low O₂ sats of the patient as the focus. - Loops do not decrease mortality in cardiac patients. They are simply used for fluid unloading for pulmonary and peripheral edema. - Can cause ototoxicity (tinnitus, vertigo). - HY point is that they can cause hypokalemia. What USMLE loves to do is tell you a patient is initiated on furosemide but it is insufficient + now needs a second diuretic → answer = anything that is potassium-sparing (i.e., ENaC inhibitor such as amiloride or triamterene; or aldosterone receptor antagonist such as spironolactone or eplerenone). - Loops ↑ urinary calcium. This is in contrast to thiazides, which ↓ it. - Ethacrynic acid is another loop you can be aware of. It is used in patients with sulfa allergies, since furosemide is a sulfa drug. It is also ototoxic.
Thiazides	<ul style="list-style-type: none"> - Hydrochlorothiazide (HCTZ) is HY example; chlorthalidone is “thiazide-like.” - Inhibit the Na⁺/Cl⁻ symporter on the apical membrane of the early-DCT. - Thiazides and dihydropyridine calcium channel blockers are used first-line for HTN in patients without any renal or cardiovascular issues. If patient has proteinuria, ↑ in creatinine or renin, or pre-diabetes or diabetes, ACEi or ARBs are used first. - Used to ↓ recurrence of calcium stones by promoting ↑ reabsorption of urinary calcium. In turn, they can sometimes cause hypercalcemia. - Can be used in heart failure in patients with diabetic nephropathy who are already on ACEi and β-blocker. Sounds specific, but there’s a new 2CK Q that has thiazide as correct over spironolactone in a diabetic. Spironolactone can cause hyperkalemia in patients who have worrisome kidney function. - Thiazides can cause gout (i.e., contraindicated in gout). - Offline NBME 20 wants you to know thiazides can cause galactorrhea (milky discharge from the nipples) via some obscure mechanism. Literature search shows it accounts for ~0.2% of adverse effects of thiazides, but count on NBME to ask it.
Amiloride, Triamterene	<ul style="list-style-type: none"> - ENaC inhibitors → block apical sodium channel in cortical collecting duct → ↓ Na⁺ reabsorption → ↓ water reabsorption. - These are potassium-sparing, which means they do not ↓ serum K⁺. This is because by inhibiting the apical ENaC channel, they indirectly inhibit the basolateral Na⁺/K⁺ ATPase → ↓ Na⁺ reabsorption + ↓ K⁺ secretion. - The answer on USMLE for a second diuretic given in a patient already on furosemide who needs additional fluid unloading. Be careful however. I’ve seen one Q where the patient is on furosemide, but the point of the Q is he/she needs HTN control, and the answer is a thiazide, not the ENaC inhibitor. You want to select an ENaC inhibitor specifically if the Q says, “We have a patient who has peripheral/pulmonary edema due to X cause + is already on furosemide; what do we do now?” → answer = amiloride or triamterene.
Spironolactone, Eplerenone	<ul style="list-style-type: none"> - Aldosterone receptor antagonists. - By blocking aldosterone receptor, it ↓ activity of the basolateral Na⁺/K⁺ ATPase → leads to indirect ↓ activity of apical ENaC → ↓ sodium reabsorption → ↓ water reabsorption. - Potassium-sparing diuretic. Same as with ENaC inhibitors, it is used for fluid unloading in patient who is already on furosemide in whom we worry about dropping their K⁺ too much.



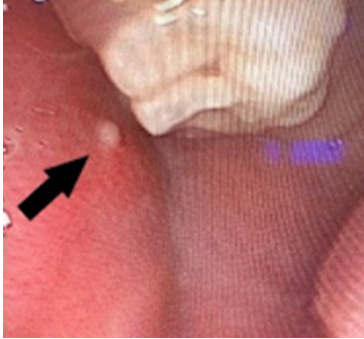
	<ul style="list-style-type: none"> - Used in heart failure up the hierarchy of meds – i.e., ACEi/ARB first-line, followed by adding β-blocker, followed by spironolactone (but if patient is diabetic with poor renal function, don't add spironolactone here; give thiazide instead as per new 2CK NBME). - Can be for aldosteronoma (Conn syndrome) prior to surgery. - Can cause gynecomastia (anti-androgenic effect by blocking androgen receptors). - Eplerenone has \downarrow risk of gynecomastia compared to spironolactone, but USMLE doesn't give a fuck. Resource masturbation garbage that's been regurgitated at times over the years.
Lisinopril	<ul style="list-style-type: none"> - USMLE-favorite ACE inhibitor. - Prevents conversion of AT-I into AT-II in the lungs. - Used for HTN in patients with pre-diabetes, diabetes, atherosclerotic disease, or renal disease (I talk about this in HY Risk Factors PDF in more detail). - Can cause dry cough (ACE is aka bradykininase, so ACEi cause \downarrow breakdown of bradykinin in lungs \rightarrow cough). - Can \uparrow serum K^+, since \downarrow aldosterone synthesis. Aldosterone normally secretes K^+ in the distal kidney). - Avoid in hereditary angioedema.
Valsartan	<ul style="list-style-type: none"> - Angiotensin II receptor blocker (ARB). - Use-cases are identical on USMLE to ACEi (i.e., if you see both as answer choices to a question, they're usually both wrong because they're the "same"). - Doesn't cause dry cough the way ACEi do.
Tolvaptan, Conivaptan	<ul style="list-style-type: none"> - ADH receptor antagonists at V2 receptor in the medullary collecting duct. - Can be used for SIADH. - Remember, however, that demeclocycline is also answer on 2CK NBME for SIADH.



IM Gastro

Disorders affecting lips/oral cavity for IM	
Peutz-Jeghers syndrome	<p>- Combination of perioral melanosis (fancy word for hyperpigmentation around the lips/mouth) + hamartomatous colonic polyps.</p>  <p>- USMLE will show image of lips pretty much always, and then they'll ask for what kind of polyps are seen in the colon (i.e., hyperplastic, tubulovillous, etc.), and the answer is just "hamartomatous."</p>
Osler-Weber-Rendu	<p>- Aka hereditary hemorrhagic telangiectasia; autosomal dominant. - NBME loves showing a mouth or fingernail picture of telangiectasias.</p>  <p>- Q will give nosebleeds + show you the above pic. There can be high-output cardiac failure due to pulmonary AV fistulae. - GI bleeding can occur leading to anemia.</p>
Plummer-Vinson syndrome	<p>- Triad of iron deficiency anemia + esophageal webs (dysphagia) + angular cheilitis (cracked corners of mouth).</p>  <p>- NBME Q can also mention pica (iron deficiency sign where patient eats clay, starch, or ice), or they can show spoon-shaped nails (koilonychia), which are a sign of severe iron deficiency.</p>

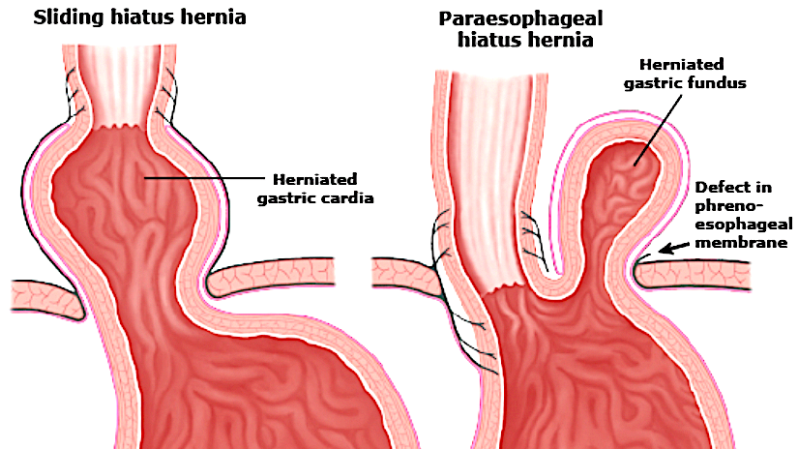
Lip psoriasis	<p>- Just know it's possible. USMLE can mention it on upper lip or forehead, and this somehow confuses students, where they think it has to be on extensors only.</p> 
Aphthous ulcer	<p>- Aka canker sore. - Usually appears as very painful lesion, self-resolving lesion on labial mucosa. - Not infective; idiopathic; thought to have very mild autoimmune association; sometimes associated with certain triggers like spicy food.</p> 
Kawasaki disease	<p>- Vasculitis that causes 5+ days of fever + injected (red) eyes and/or lips/tongue + cervical lymphadenopathy + edema of dorsa of the hands + desquamation of palms/soles (often mentioned as palms/soles "rash," but not true rash).</p>  <p>- Students obsess over coronary artery aneurysms as though they're so HY. They're not. USMLE basically never mentions them.</p>
Perioral impetigo	<p>- Often confused with herpes.</p> 

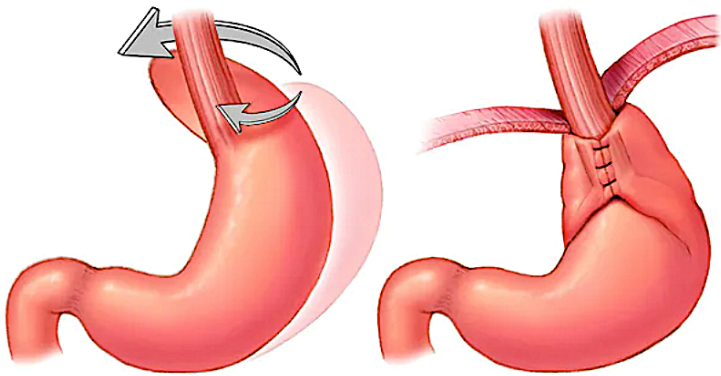
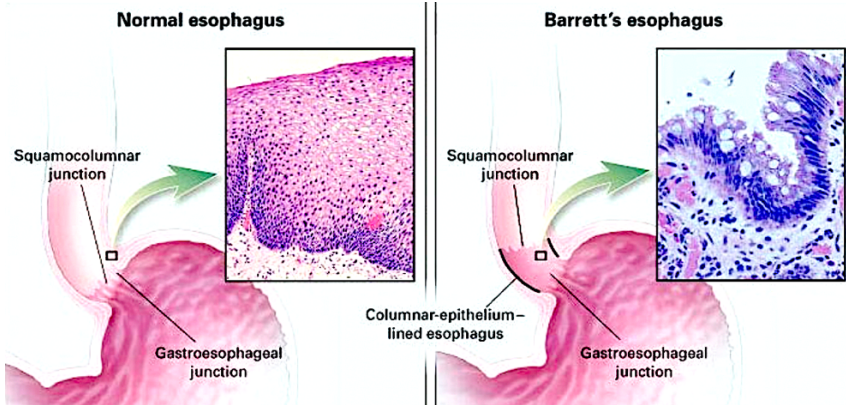
	<ul style="list-style-type: none"> - If they show you image of young kid in particular with lip lesions, it's usually impetigo caused by <i>S. aureus</i> or Group A Strep (<i>S. pyogenes</i>). - Can lead to PSGN (if caused by Strep), as discussed in the HY Renal PDF.
Herpes labialis	<ul style="list-style-type: none"> - Caused by HSV1 or 2. USMLE doesn't give a fuck about HSV1 being the lips and HSV2 being the genitals. Bunch of nonsense perpetuated by other resources.  <ul style="list-style-type: none"> - Primary infection presents with fever and regional lymphadenopathy. Recurrences aren't as severe. - HSV goes latent in sensory nerves. - USMLE will show you above pic and then the answer is "DNA, enveloped, linear." Sounds nitpicky and low-yield, but it's one of the viral structures they like asking. Don't confuse with HepB, which is "DNA, enveloped, circular." I've made lots of YouTube clips on that stuff. - Treat with acyclovir → DNA polymerase inhibitor causing chain termination. HSV resistance to it will be due to altered thymidine kinase.
Scarlet fever	<ul style="list-style-type: none"> - Caused by Group A Strep. - Causes strawberry tongue / red lips + salmon-pink maculopapular body rash.  <ul style="list-style-type: none"> - Treatment is penicillin to prevent rheumatic fever (type II HS); can also lead to PSGN (type III HS). I discussed this stuff in the HY Cardio and Renal PDFs.
Hand-foot-mouth	<ul style="list-style-type: none"> - Caused by Coxsackie A (an RNA virus under picornaviridae). - Causes benign, but contagious, lesions on, you guessed it LOL! – the hands, feet, and mouth. - Usually pediatric, but can present in adults (i.e., daycare workers, parents).  <ul style="list-style-type: none"> - Don't confuse with coxsackie B, which can cause dilated cardiomyopathy, diabetes type I, and pleurodynia (latter I discussed in HY Pulm PDF).

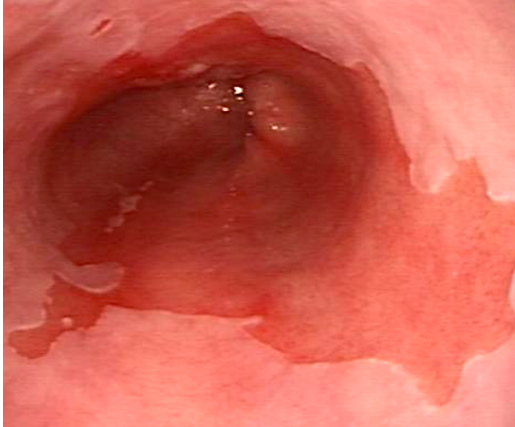
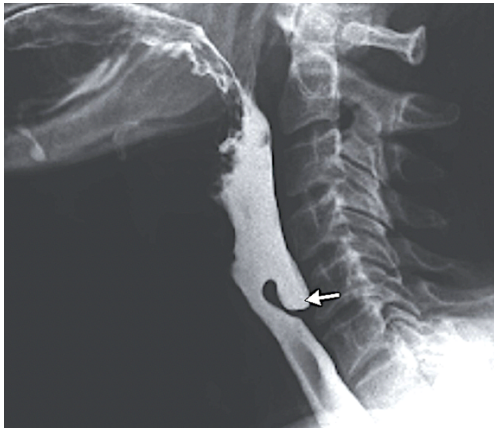
Herpangina	<ul style="list-style-type: none"> - Also caused by coxsackie A. - Presents as oropharyngeal vesicles or sores. 
Koplik spots	<ul style="list-style-type: none"> - Can occur with or without hand-foot-mouth. - Caused by measles. - White/blue-ish spots on buccal mucosa.  <ul style="list-style-type: none"> - One of the ways to distinguish measles (rubeola) from rubella (German measles). - The same way you can memorize Koplik spots as unique to measles, you should memorize sub-occipital and post-auricular lymphadenopathy as unique to rubella. - Both measles and rubella have a head-to-toe maculopapular body rash. - Both can present with fever, cough, coryza, conjunctivitis. These findings are non-specific for viral infection; it's been erroneously attributed to only measles over the years, but I've it show up in numerous NBME Qs for a variety of viruses).
Sialolithiasis	<ul style="list-style-type: none"> - Stones within the ducts of the salivary glands. - Stensen duct is the opening of the parotid duct (from parotid gland) into the oral cavity, which is located near the 2nd upper molar bilaterally.  <ul style="list-style-type: none"> - Sometimes a Q can say a patient has pain or inflammation on the buccal mucosa across from the second upper molar, and sialadenitis (inflammation) or sialolithiasis can be an answer.
Leukoplakia	<ul style="list-style-type: none"> - White-ish, painless, rough patch on lateral tongue.

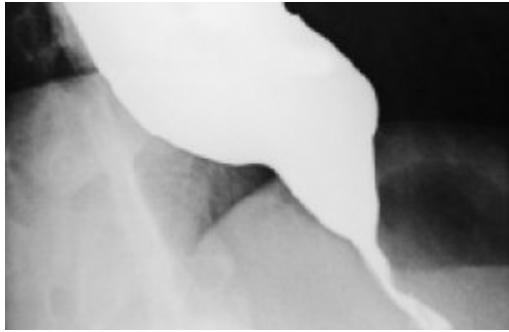
	 <ul style="list-style-type: none"> - Precursor to squamous cell carcinoma of tongue. - Biggest risk factor is smoking / chewing tobacco.
Oral hairy leukoplakia	<ul style="list-style-type: none"> - Looks like leukoplakia, but caused by EBV. - Not considered premalignant (no dysplasia on biopsy).
Oropharyngeal candidiasis	 <ul style="list-style-type: none"> - Painless white plaque on palate or tongue that bleeds when scraped. - Seen in immunocompromised patients, such as AIDS or organ transplant recipients on immunosuppressant agents. - Can be seen in patients with asthma who use inhaled corticosteroids. Patients need to rinse their mouths with water after use to ↓ candida risk. - Tx with nystatin mouthwash. - Odynophagia (painful swallowing) in an immunocompromised patient is Candidal esophagitis until proven otherwise.

Salivary gland neoplasia	
Pleomorphic adenoma	<ul style="list-style-type: none"> - The answer on USMLE for benign salivary gland tumor that has variability in cell size and shape. - Most common salivary gland tumor; benign. - Pleomorphic = cells and nuclei have variability in size and shape.
Mucoepidermoid carcinoma	<ul style="list-style-type: none"> - The answer on USMLE for a salivary gland tumor that invades / has spread / if the patient has B-symptoms (fever, night sweats, weight loss). - Most common <i>malignant</i> salivary gland tumor. - Malignant means capable of invading, whereas pleomorphic adenoma will not invade.
Warthin tumor	<ul style="list-style-type: none"> - The answer on USMLE for salivary gland tumor where they say anything about it resembling lymphatic tissue. - Salivary gland tumor that has lymphoid stroma (i.e., looks like lymphatic tissue).



HY Esophageal conditions for IM	
Hiatal hernia	<ul style="list-style-type: none"> - Herniation of the stomach upward through the diaphragm. - 95% of the time, hiatal hernia is known as “sliding,” where the cardia of the stomach rises upward through the esophageal hiatus (opening in diaphragm where esophagus passes). - “Abnormal relation of the cardia to the lower end of the diaphragm” is answer on NBME. - 5% of the time, it is paraesophageal, where the fundus of the stomach herniates upward through a hole in the diaphragm adjacent the esophagus. - “Protrusion of the fundus into the chest above the level of T10” = answer for paraesophageal hernia on NBME.  <p>The diagram illustrates two types of hiatal hernia. On the left, 'Sliding hiatal hernia' shows the stomach's cardia (lower esophageal sphincter) sliding up through the diaphragm. On the right, 'Paraesophageal hiatal hernia' shows the stomach's fundus (upper part) herniating through a separate opening in the diaphragm, adjacent to the esophagus. Labels include 'Herniated gastric cardia' for the sliding type and 'Herniated gastric fundus' and 'Defect in phreno-esophageal membrane' for the paraesophageal type.</p> <ul style="list-style-type: none"> - Often associated with gastroesophageal reflux disease (GERD). - Surgery usually not indicated. - Diagnose with upper endoscopy (asked on 2CK Surg).
Gastroesophageal reflux disease (GERD)	<ul style="list-style-type: none"> - Irritation of esophageal mucosa by gastric acid; usually caused by ↓ lower esophageal sphincter (LES) tone. - USMLE wants you to know obesity is a risk factor for GERD, likely due to ↑ stretching and pressure applied to the LES. - As mentioned above, hiatal hernia is also a risk factor. - Classic presentation is burning in the throat/chest after eating a meal. - Can present with nocturnal cough or recurrent pneumonitis. These are HY findings in patients who don't have classic esophageal irritation symptoms. - Can lead to Barrett esophagus (discussed below), which leads to esophageal adenocarcinoma. - First step in diagnosis is 2-week trial of proton pump inhibitor (PPI), such as omeprazole, which will ↓ symptoms. - PPIs are more efficacious than H2-blockers (e.g., cimetidine). If you see both a PPI and H2-blocker as answers for a GERD Q, choose the PPI. - One 2CK form has “2-week trial of H2-blocker” as an answer, but PPI isn't listed, so just know the Q is out there. - If trial of PPI doesn't work, 24-hour esophageal pH monitoring is the answer. - Nissen fundoplication is used last resort, but is asked on NBMEs.

	<p>Nissen fundoplication</p>  <p>A. Fundus wrapped around back side of esophagus</p> <p>B. Wrap secured with sutures to anchor lower esophagus below diaphragm</p> <ul style="list-style-type: none">- Answer can be written as “fundoplication” alone in patient with severe GERD. This also shows up on Peds, where they say infant with severe GERD and fundoplication is answer.- Pediatric GERD will present as coughing up milk 2-3x daily. It will not be described as high-energy or forceful (i.e., pyloric stenosis); it will not be bilious (i.e., duodenal atresia; annular pancreas); it will not occur as choking or spitting up during the first feed (i.e., tracheoesophageal fistula).- Answer to pediatric GERD Q is “immature lower esophageal sphincter”. It’s not complicated, but I’ve seen students say, “Wait, you can get GERD in kids?”- Tx for pediatric GERD is thickened feeds (addition of dry rice to formula) and positional change prior to any use of PPIs.
Barrett esophagus	<ul style="list-style-type: none">- Metaplasia of distal esophagus characterized by conversion of non-keratinized stratified squamous epithelium into columnar epithelium with goblet cells (which secrete mucous).- You’ll sometimes here the latter described as “intestinal columnar epithelium.” This is because the stomach doesn’t have goblet cells; it has mucous neck (foveolar) cells.- Major risk factor for esophageal adenocarcinoma. 

	 <ul style="list-style-type: none"> - Can appear grossly red on upper endoscopy. Once visualized, the next best step is biopsy to confirm the presence of Barrett metaplasia.
Adenocarcinoma	<ul style="list-style-type: none"> - Affects lower 1/3 of esophagus. - HY pathogenesis is: GERD → Barrett esophagus → adenocarcinoma. - Will present in patient over 50 who has Hx of GERD with either 1) new-onset dysphagia to solids, or 2) dysphagia to solids <i>that progresses</i> to solids and liquids. - The “new-onset dysphagia” can refer to 3-6-month Hx in patient with, e.g., 10-20-year Hx of GERD. - 2CK wants immediate endoscopy in either of the above situations (i.e., don’t choose barium first). - Sometimes rather than making you choose endoscopy straight up, they’ll tell you in the last line an endoscopy was performed and shows a stricture, then they’ll ask for next best step → answer = biopsy of the stricture.
Squamous cell carcinoma	<ul style="list-style-type: none"> - Affects upper 2/3 of esophagus. - Biggest risk factors for USMLE are heavy smoking/alcohol use. - Other risk factors like burns, chemicals, achalasia, etc., are nonsense. - Will present in patient over 50 who is heavy smoker/drinker who has 1) new-onset dysphagia to solids, or 2) dysphagia to solids <i>that progresses</i> to solids and liquids. - Same as with adenocarcinoma, USMLE wants immediate endoscopy as the answer, followed by biopsy of a stricture or lesion if present.
Zenker diverticulum	<ul style="list-style-type: none"> - Outpouching of esophagus above the cricopharyngeus muscle (just above the upper esophageal sphincter).  <ul style="list-style-type: none"> - Mechanisms on USMLE are numerous and include, “cricopharyngeal muscle spasm,” “uncoordinated swallowing,” “dysphagia,” and “increased oropharyngeal pressure.”

	<ul style="list-style-type: none"> - False diverticulum (contains only mucosa + submucosa; true diverticula, in contrast, such as Meckel, include the muscular layer as well). - Often presents as overweight male over 40-50 with gurgling sounds when swallowing, or regurgitation of undigested food. - Halitosis (bad breath) is buzzy but only mentioned in maybe 1/3 of Qs. - Diagnosis is made with barium swallow. - Treatment on 2CK NBME is "diverticulectomy."
Achalasia	<ul style="list-style-type: none"> - Tightening (i.e., ↑ tone) of the LES due to loss of NO-secreting neurons in the Auerbach (myenteric) plexus. - New NBME wants "enteric ganglia" as the answer for site of problem. - Can be described on NBME as "dilated esophagus with constriction of the gastroesophageal junction." - Presents usually as dysphagia to both solids and liquids from the start. This is in contrast to cancer, which will be new-onset dysphagia to just solids, or <i>progression</i> from solids only to solids + liquids. The HY point is that neurogenic causes of dysphagia (i.e., achalasia) lead to solids + liquids dysphagia. - Almost always idiopathic; can rarely be caused by Chagas disease. - New 2CK NBME has "South American trypanosomiasis" as the answer for achalasia, which is aka Chagas disease. - First step in diagnosis is barium swallow, which shows a classic "bird's beak" appearance.  <ul style="list-style-type: none"> - After the barium is performed, esophageal manometry (a pressure study) is confirmatory. Biopsy is not traditionally performed. - Treatment is pneumatic (balloon) dilation, followed by myotomy (cutting of muscle fibers of the LES).
Systemic Sclerosis (aka scleroderma)	<ul style="list-style-type: none"> - As discussed in detail in the HY Pulm PDF, this is an idiopathic autoimmune disease characterized by multi-organ system fibrosis and hardening of tissues (i.e., sclerosis). - Can lead to GERD. NBME wants ↓ LES sphincter tone and ↓ esophageal peristalsis as an answer. This refers to the esophageal dysmotility component of CREST (Calcinosis, Raynaud's, Esophageal dysmotility, Sclerodactyly, Telangiectasias).
Esophageal perforation	<ul style="list-style-type: none"> - Can either be iatrogenic (i.e., from endoscopy) or Boerhaave syndrome (from increased pressure due to retching, vomiting, or straining). - USMLE likes to say water-soluble contrast swallow shows accumulation in the mediastinum. If they don't mention this, they'll give either recent endoscopy or straining + acutely low BP and high HR, where you have to eliminate the other answers out of reasoning. - Water-soluble contrast (Gastrografin) is used in suspected perforation because the contrast will leak into the mediastinum and barium can cause mediastinitis. - In contrast (no pun intended), if patient has aspiration risk, we use barium and not Gastrografin because the latter can cause pneumonitis. - "Esophageal repair" is the Tx on NBME. Pretty straightforward.

Mallory-Weiss tear	<ul style="list-style-type: none"> - Classically retching/vomiting in an alcoholic that causes stretching and tearing of the gastroesophageal junction leading to small amounts of blood in vomitus. - Can also occur in patients with eating disorders or hyperemesis gravidarum. - It's to my observation on NBME material that the highest yield point about MW tear is that it does not cause high-volume hematemesis. If the vignette mentions high-volume blood, that is ruptured varix instead (discussed below).
Esophageal varices	<ul style="list-style-type: none"> - Enlarged and tortuous superficial esophageal veins due to portal hypertension in patient with cirrhosis or splenic vein thrombosis. <div data-bbox="759 517 1155 851" data-label="Image"> </div> <div data-bbox="533 878 1378 1240" data-label="Image"> </div> <ul style="list-style-type: none"> - The mechanism in the setting of cirrhosis: the left gastric vein connects the esophageal veins to the portal vein. In the setting of \uparrow portal pressure, this pressure backs up to the left gastric vein, which backs up to the esophageal veins. Many USMLE Qs want "left gastric vein" as the answer for the vessel responsible for the varices. - In splenic vein thrombosis, the \uparrow splenic venous pressure causes formation of collaterals to circumvent the thrombosis. This means nearby veins will form small tributaries/branches from the splenic vein. The left gastric vein is one of them \rightarrow \uparrow esophageal venous pressure. - It is to my observation on NBME Qs that 4/5 varices Qs will give a patient with high-volume hematemesis. In contrast, MW tear is "just a little blood." - Ruptured varices are lethal ~50% of the time. The patient will vomit high volumes of blood. - 1/5 Qs might say "just a little blood" if the varix is friable but not overtly ruptured, but the vignette will be obvious (i.e., cirrhosis) + they might just ask for "left gastric vein" as the answer. - Propranolol is prophylaxis, not for acute treatment. - Treatment is endoscopy + banding. - Octreotide can also be used for acute bleeding, but endoscopy + banding is best answer on USMLE if you are forced to choose. - There is a 2CK Q where patient has $\downarrow\downarrow$ BP due to ruptured varix and the answer is "IV fluids," where endoscopy is the wrong answer. I've had a student say, "Wait but I thought you said endoscopy and banding is what we

	do first.” And my response is, yeah, but you always have to address ABCs first on 2CK. They could by all means say patient has O2 sats of 50% and the answer would be give oxygen before fluids.
Diffuse esophageal spasm	<ul style="list-style-type: none"> - Idiopathic spasm of the esophagus. - All you need to know is that this that causes pain that can mimic angina pectoris, but patient will be negative for cardiac findings/disease.  <ul style="list-style-type: none"> - Barium shows a corkscrew appearance. - “Nutcracker esophagus” is a similar condition that is due to idiopathic hyperperistalsis and causes pain similar to DES.
Eosinophilic esophagitis	<ul style="list-style-type: none"> - Idiopathic allergic condition of the esophagus that presents with difficulty swallowing. - Biopsy shows eosinophils in epithelium (it’s like no shit).  <ul style="list-style-type: none"> - Endoscopy shows “trachealization” of the esophagus with concentric rings. - Patient might have history of asthma or atopy.
Schatzki ring	<ul style="list-style-type: none"> - Garbage diagnosis for USMLE. Doesn’t exist. Mentioning it here as a negative for USMLE giving a fuck cuz otherwise someone will be like, “Mike u didn’t mention Schatzki ring.” - Technically a narrowing of the distal esophagus that could be considered as a differential alongside achalasia. Once again, never seen this assessed as a correct answer on any NBME material. Maybe just once as a distractor. Garbage diagnosis.

HY GI endocrine hormones quick review	
Insulin	<ul style="list-style-type: none"> - Produced by β-islet cells in the tail of pancreas. - \downarrow blood glucose by two main mechanisms: 1) \uparrow GLUT-4 on skeletal muscle and adipose tissue; 2) \uparrow glucokinase activity in the liver (hexokinase equivalent at liver), which pulls glucose out of the blood to be stored as glycogen. - \uparrow Fatty acid and protein synthesis. Also \uparrow lipoprotein lipase activity (fat storage). - Causes dephosphorylation of enzymes (I talk about this in detail in my HY Biochem pdf). - Insulin secretion is HY: glucose enters β-islet cells via GLUT-2 \rightarrow \uparrow ATP production within β-islet cell \rightarrow closure of ATP-gated K^+ channel on membrane of β-islet cell \rightarrow K^+ builds up

	<p>inside the cell → more positive charge in cell → depolarization of cell → causes Ca^{2+} to move into cell → triggers insulin vesicle efflux from cell.</p> <ul style="list-style-type: none"> - Insulin is normally produced as pro-peptide that must have C-peptide cleaved off as part of the process. C-peptide and insulin are co-secreted, meaning their serum levels should match one another. If patient has ↑ insulin but ↓ C-peptide, answer = exogenous injection. If C-peptide is normal/high, insulin production is endogenous. First step is checking serum hypoglycemic levels ("serum hypoglycemic" = type II diabetes med that ↓ glucose, such as sulfonylureas and meglitinides). If serum hypoglycemics are negative, then do CT of abdomen to check for insulinoma. - Insulinoma (and ↑ insulin in general) cause Whipple triad: 1) hypoglycemia; 2) symptoms of hypoglycemia (tachycardia, tremulousness); 3) improves with a meal / gets worse between meals. - Insulin is absent in type I diabetes and ↑↑ in early type-II diabetes (i.e., hyperinsulinemia). - Insulin inhibits ketone formation, so we have ↓ ketones in type II, but ↑ ketones in type I. - Hyperinsulinemia causes anovulation / polycystic ovarian syndrome (see my Repro PDF). - USMLE can show you pic of acanthosis nigricans, which is almost always due to insulin resistance. - Patients with chronic pancreatitis and pancreatectomy can have diabetes (loss of pancreatic tail).
Glucagon	<ul style="list-style-type: none"> - Secreted by α-cells of the pancreatic tail. - Causes ↑ serum glucose and phosphorylation of enzymes. - Glucagonoma will present as ↑ serum glucose and a body rash called necrolytic migratory erythema. Don't confuse with the facial flushing seen with VIPoma; in addition, VIPoma doesn't ↑ glucose levels. - Patients who receive insulin for diabetes can sometimes have prolonged or exaggerated hypoglycemic effects. If this occurs, an answer for why this occurs on USMLE is "lack of counter-regulatory glucagon." Sounds weird, but it shows up more than once on NBMEs. Essentially, patients with diabetes, or chronic pancreatitis, or pancreatectomy and not just prone to losing the β-islet cells, but they can also lose the α-cells. When glucose goes ↓, glucagon should go ↑ to compensate, but if this can't happen, glucose stays low. - Question on NBME with chronic pancreatitis (chronic burnout from repeated acute pancreatitis; discussed more later) wants you to know that the arrows are: ↓ insulin production, ↓ glucagon production, no-change peripheral response to insulin.
Somatostatin	<ul style="list-style-type: none"> - Secreted by delta-cells of pancreatic tail. - ↓ secretion of most GI hormones, as well as growth hormone. - Somatostatinoma presents as steatorrhea (probably due to ↓ pancreatic lipase secretion). - Octreotide is a somatostatin analogue that can be used in addition to endoscopic banding for esophageal varices Tx → leads to ↓ portal blood flow/pressure.
Ghrelin	<ul style="list-style-type: none"> - Produced by enteroendocrine cells of GI tract. - All you need to know is that this hormone makes you feel hungry. - Blood levels are highest just at the start of the meal. USMLE will show you a graph of ghrelin levels, and they ask where on the graph corresponds to the start of a meal, and the answer is at the peak. Not complicated. But I've seen innumerable students get this wrong.
Leptin	<ul style="list-style-type: none"> - Produced mostly by adipocytes. - Makes you feel full (i.e., opposite of ghrelin). - Also plays important role in hypothalamic/anterior pituitary secretion of gonadotropins. - Leptin is ↓ in those with low BMI/anorexia → ↓ GnRH → ↓ LH + ↓ FSH → amenorrhea.

Peptic ulcers HY causes	
<ul style="list-style-type: none"> - "Peptic ulcer" is an umbrella term that refers to both duodenal and gastric ulcers. - Gastric ulcers cause pain immediately with meals (due to \uparrow acid secretion). Patients can sometimes lose weight due to aversion to pain from eating. - Duodenal ulcers cause pain 1-2 hours after meals (due to \uparrow acid entering duodenum). With meals, the pylorus tightens, thereby relieving any residual discomfort. Patients may gain weight since eating \downarrow pain. 	
<i>Helicobacter pylori</i>	<ul style="list-style-type: none"> - Responsible for almost all duodenal ulcers (>95%), whereas it causes a lower % (only >60%) of gastric ulcers. This is merely because the latter are caused by many other things as well, so we simply have \downarrow fraction caused by <i>H. pylori</i>. In other words, there's no special tropism of <i>H. pylori</i> toward duodenal over gastric mucosa. - Mechanism for ulcers that shows up on USMLE is: "secretes proteinaceous substrates that damage mucosal lining." This is correct over "\uparrow gastric acid secretion" if both are listed side-by-side, even though <i>H. pylori</i> does \uparrow gastrin levels, which \uparrow acid secretion. - Produces urease, which causes \uparrow ammonia production around the organism, allowing it to survive in the \downarrow pH of the stomach. - Antral/pyloric ulcers can lead to gastric outlet obstruction. They will mention this in a Surg Q as a "succussion splash." - \uparrow risk of MALT lymphoma, a type of B-cell lymphoma. - Diagnose <i>H. pylori</i> with urease breath test or stool antigen. - Treat <i>H. pylori</i> with CAP \rightarrow clarithromycin, amoxicillin, PPI (e.g., omeprazole). - USMLE really doesn't give a fuck about the treatment, but CAP is safe to know. Metronidazole, tetracycline, bismuth, and PPI tetrad is used if CAP fails (students ask about those other drugs). - Perforated duodenal ulcer will present as sudden-onset rigid abdomen (involuntary guarding). Patient will often have SIRS, with abnormal vitals due to sympathetic activation. USMLE wants "X-rays of the chest and abdomen" to look for air under the diaphragm (HY finding that indicates ruptured viscus).
Gastrinoma	<ul style="list-style-type: none"> - Zollinger-Ellison syndrome causes recurrent duodenal ulcers and sometimes jejunal or ileal ulcers. - Can be part of MEN1 or idiopathic. - <i>H. pylori</i> is more common than gastrinoma. As mentioned above, >95% of duodenal ulcers are due to <i>H. pylori</i>. There is an NBME Q where they give older male with a duodenal ulcer + no other information + they ask for most likely cause \rightarrow answer = testing for <i>H. pylori</i>; gastrinoma is wrong. - Vignettes can be tricky with gastrinoma and tell you the patient has 8-10 watery stools daily, where you say, "That sounds like VIPoma." But they'll also tell you the patient has history of abdo pain after meals. Q on IM form 8 does this as example.
NSAIDs	<ul style="list-style-type: none"> - Cause gastric ulcers. I haven't seen these cause duodenal ulcers on USMLE. - Prostaglandins are necessary for stimulation of gastric alkaline mucous production and maintenance of the gastric lining. NSAIDs \rightarrow \downarrow prostaglandin production \rightarrow disruption of gastric lining. This can lead to both ulcers and irritation (gastritis). - USMLE wants you to know that PPIs are first-line for ulcer treatment in general, but that misoprostol is a PGE1 analogue that is used in NSAID-induced ulcers (i.e., we're replenishing the \downarrow prostaglandin from NSAIDs).
Burns	<ul style="list-style-type: none"> - Rare, but just know they exist. - Called Curling ulcers (think: curling irons are hot). - Loss of fluid post-burns from evaporation \rightarrow \downarrow blood flow to stomach \rightarrow ischemic ulcers.
Head trauma	<ul style="list-style-type: none"> - Rare, but just know they exist. - Head trauma or brain tumor \rightarrow \uparrow intracranial pressure \rightarrow \uparrow parasympathetic outflow to stomach \rightarrow \uparrow ACh binding to muscarinic receptors at parietal cells \rightarrow \uparrow acid production. - Don't forget that the 3 synergistic mechanism for acid production are 1) gastrin binding directly to gastrin receptors on parietal cells; 2) gastrin stimulating enterochromaffin-like cells to secrete histamine, which then binds to H2 receptors on

	parietal cells; and 3) direct parasympathetic activity, where ACh binds to muscarinic receptors on parietal cells.
Smoking/Alcohol	- Not tested as overt causes of ulcers on USMLE. But you should know that smoking and alcohol are believed to <i>decrease healing</i> of pre-existing ulcers.

Gastritis causes + HY points	
	<ul style="list-style-type: none"> - Acute gastritis will present as irritation leading to bleeding of gastric mucosa (e.g., from NSAIDs). - Chronic gastritis will be an atrophy or autoimmune destruction of the mucosa associated with ↓ mucosal thickness, ↓ HCl production (achlorhydria), ↑ gastrin production, and enterchromaffin-like cell hyperplasia (↑ histamine production to compensate for ↓ acid). NBME will give you this constellation of findings and then just simply have “chronic gastritis” as the answer, with acute gastritis not even listed. It’s not hard, but I’ve seen students miss this a lot.
<i>H. pylori</i>	<ul style="list-style-type: none"> - Causes what is referred to as “Type B gastritis,” which is inflammation tending to affect the antrum of the stomach. - Can lead to pyloric channel ulcers + gastric outlet obstruction. This will present on 2CK forms as a “succussion splash.”
Pernicious anemia	<ul style="list-style-type: none"> - Causes what’s referred to as type A gastritis,” which affects mostly the fundus/body of the stomach. - Autoimmune antibody-mediated destruction of parietal cells. - Sometimes antibodies can be against intrinsic factor. - Ultra-HY cause of B12 deficiency (↑ MCV + hypersegmented neutrophils +/- neuropathy) on USMLE. - Associated with other autoimmune diseases, e.g., vitiligo. So if they give you ↑ MCV in patient with, e.g., type I diabetes, you should think, “Autoimmune diseases go together, so if the patient has one AA disease, he/she has ↑ propensity for others.” Don’t worry about strict HLA associations here.
NSAIDs	<ul style="list-style-type: none"> - Answer on USMLE for GI bleeding in someone taking, e.g., indomethacin or naproxen. - Causes type A gastritis, affecting the fundus/body. USMLE doesn’t specifically give a fuck, but you should basically be like, “<i>H. pylori</i> causes antral gastritis, whereas other causes like NSAIDs and pernicious anemia are fundus/body of stomach.” - Prostaglandins are necessary for stimulation of gastric alkaline mucous production and maintenance of the gastric lining. NSAIDs → ↓ prostaglandin production → disruption of gastric lining. This can lead to both gastritis (inflammation) and ulcers. - As mentioned above for ulcers, misoprostol can be used in these patients following PPI.

Gastric cancer points
<ul style="list-style-type: none"> - Perpetuated over the years as “intestinal vs diffuse” types. USMLE doesn’t care. What you need to know is that histo will show signet-ring cells that contain mucin. And you don’t need to know the histo for this either. - Grossly, can cause a linitis plastica, which is a leather bottle appearance to the stomach. - Gastric metastases can spread hematogenously to the ovaries. These will show up as bilateral ovarian lesions that show, you guessed it, signet-ring cells that contain mucin. - ↑ incidence of gastric cancer in Japan due to ↑ nitrosamines/smoked foods. - MALT lymphoma is a B cell lymphoma that can be caused by <i>H. pylori</i>. This does not have signet ring cells. - Acanthosis nigricans can be associated with gastric cancer (even though most of the time, it just means insulin resistance). - Virchow node (Troisier sign) → palpable supraclavicular lymph node that can reflect visceral malignancy, especially gastric cancer.

Hyperbilirubinemia	
Unconjugated (indirect)	<ul style="list-style-type: none"> - Bilirubin is produced from breakdown of heme from RBCs at the spleen. It will initially be “unconjugated” in this form, where it merely leaves the spleen non-covalently bound to albumin and is not water-soluble – i.e., it won’t show up in the urine. Unconjugated bilirubin is aka indirect bilirubin. - In the setting of hemolysis or ↑ RBC turnover (i.e., sickle cell, hereditary spherocytosis, blood given during surgery), where we have ↑ RBC breakdown, we get ↑ indirect bilirubin. - Once it arrives at the liver, it is taken up by the liver and conjugated to glucuronide, making it water-soluble. Conjugated bilirubin is aka direct bilirubin. - If there’s a problem with uptake at the liver (i.e., acute hepatitis), or there is deficient conjugation enzyme (Gilbert syndrome, Crigler-Najjar), indirect bilirubin also goes ↑. - Hemolysis or ↑ RBC turnover can cause direct bilirubin to go ↑ sometimes as well, but the shift will be more toward indirect being ↑. I point this out because students often get confused by this, but if we have ↑ indirect bilirubin going into the liver, then this means ↑ direct bilirubin going out. A 2CK NBME Q gives 9 packs of RBCs given during surgery → days later, total bilirubin is 5.0 and direct bilirubin 2.3 → answer = “overproduction of bilirubin.” - In regard to neonatal labs (i.e., first month of life), I should note that hematocrit % can be in the 50s (NR 45-61; in adults, NR is 40-50). 2CK, for instance, will often show Hct as 56% in a newborn and the student is like “Wow that’s high!” where they think there’s neonatal polycythemia or some other pathology, but it’s actually normal. Unconjugated jaundice can occur in neonates because of ↑ RBC turnover where HbF is replaced with HbA.
Conjugated (direct)	<ul style="list-style-type: none"> - Direct bilirubin, since it is water-soluble, shows up in the urine. It will also be secreted into bile. Therefore, if we have a bile duct obstruction, we get ↑ direct bilirubin. ALP also goes ↑ in bile duct obstruction because it is secreted by bile duct epithelium. This means “↑ ALP + ↑ direct bilirubin” is very buzzy for bile duct obstruction. If ALP is high but direct bilirubin not ↑, this can be due to things like bone fractures or Paget disease. - GGT will also go up with bile duct obstruction, since it is also secreted by bile duct epithelium, but USMLE actually rarely mentions this one. What they want you to know is GGT spikes with acute alcohol consumption / binge drinking. - In the event of bile duct obstruction, not only will ALP and direct bilirubin go ↑, but the urine becomes darker from ↑ direct bilirubin in it (and urobilin, which comes from direct bilirubin, but USMLE doesn’t assess this). In addition, stools become lighter/pale (aka “acholic stools”), since there is ↓ direct bilirubin making it to the intestines, which means ↓ stercobilin production (pigmentation in stool). In other words, “dark urine + pale stools” is buzzy for bile duct obstruction the same way “↑ ALP and ↑ direct bilirubin” is. - Acute hepatitis can also cause ↑ direct bilirubin due to ↓ secretion into bile, in addition to ↑ indirect. But this makes sense, since it is literally an intra-hepatic pathology. - Highest yield cause of ↑↑ direct bilirubin on USMLE is biliary atresia in neonates (discussed later). This is all over the place, whereas Crigler-Najjar (↑↑ indirect bilirubin in neonates) is nonexistent. - Dubin-Johnson and Rotor syndromes are virtually nonexistent on USMLE but cause ↑ direct bilirubin in adults due to ↓ bile excretory pumps at the liver. Students get hysterical about these because they sound weird, but they’re LY. Dubin-Johnson is asked once on a new 2CK NBME form. But apart from that, LY. - Cholangitis (inflammation of bile ducts), choledocholithiasis (stone in biliary tree), choledochal cyst, head of pancreas cancer (impingement on common bile duct), and cholangiocarcinoma (bile duct cancer) are all HY causes of bile duct obstruction. I discuss all of these conditions in detail below.

Bilirubin uptake/secretion diseases	
Gilbert	<ul style="list-style-type: none"> - Pronounced “Jeel-BEAR, not “GILL-burt.” Gastroenterologist I met once tripped out over med students pronouncing this wrong. - Partial deficiency of bilirubin uptake enzyme at the liver (UDP glucuronosyltransferase).

	<ul style="list-style-type: none"> - Presents as isolated ↑ indirect bilirubin with yellow eyes in young adult with stress factor, such as studying for exams, or recent surgery/trauma. The patient will otherwise be completely healthy. - No treatment necessary.
Crigler-Najjar	<ul style="list-style-type: none"> - Near-absence of UDP-glucuronosyltransferase causing ↑↑ indirect bilirubin in neonate. - Nonexistent yieldness but students ask about this.
Dubin-Johnson	<ul style="list-style-type: none"> - ↓ excretion of bilirubin into bile at the liver due to ↓ secretory pumps. - Causes ↑ direct bilirubin in otherwise healthy adult. - Can cause black liver in theory. - Asked once on new 2CK NBME. Apart from that, nonexistent on USMLE material.
Rotor	<ul style="list-style-type: none"> - Same as Dubin-Johnson but no black liver. - Nonexistent diagnosis on USMLE. Students get maniacal over this supposedly not having a black liver, whereas Dubin-Johnson has a black liver – “Rotor! That’s the one that has no black liver but Dubin-Johnson does!” Relax. Take two steps back, chill the fuck out for two seconds. USMLE doesn’t give a fuck.
Biliary atresia	<ul style="list-style-type: none"> - One of the highest yield Peds diagnoses. Answer on USMLE for ↑↑ direct bilirubin in a kid under the age of 6 weeks. - Caused by lack of development of the intrahepatic bile ductules and biliary tree. - Ultrasound will be done first, but USMLE wants liver biopsy to confirm the diagnosis. - Kasai procedure is done to treat, followed by liver transplant if unsuccessful.

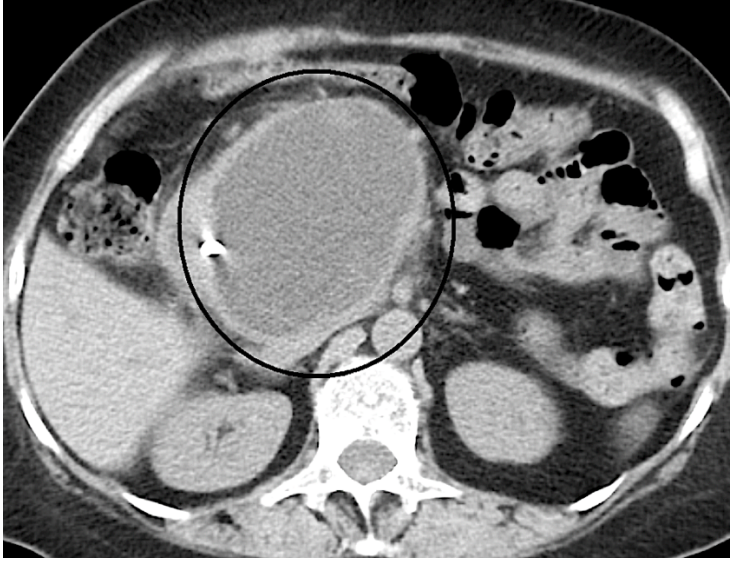

Autoimmune liver conditions	
Primary biliary cirrhosis	<ul style="list-style-type: none"> - Inflammation of bile ducts within the liver, leading to their destruction. - Answer in a woman 20s-50s who has generalized pruritis, ↑ serum cholesterol, ↑ ALP, ↑ direct bilirubin. - USMLE loves to mention Hx of autoimmune disease in the patient or family member (because autoimmune diseases go together). So they’ll say she has type I diabetes mellitus, SLE, or vitiligo; or her brother has RA, etc. - They can mention a stone is present in the gallbladder on ultrasound, which gets some students real emotional / confused, but it makes sense since patient has ↑ cholesterol. It’s just a distractor point and doesn’t relate to the actual diagnosis at hand. - Diagnose with anti-mitochondrial antibodies as first step, followed by liver biopsy to confirm. - Initial Tx = ursodeoxycholic acid (ursodiol). - New NBME material asks a couple Qs on fat-soluble vitamin malabsorption for PBC (deficiency of A and D on NBME for each Q, respectively, with no info supporting those presentations; they just ask for hypothetical vitamin deficiency). In theory, would be due to biliary obstruction, where ↓ bile entering small bowel merely means ↓ fat absorption. This is nothing special to PBC, but I mention it because it’s asked twice.
Autoimmune hepatitis	<ul style="list-style-type: none"> - Young adult with ↑ LFTs who has (+) anti-smooth muscle antibodies.

HY Hepatobiliary conditions	
Pancreatic cancer	<ul style="list-style-type: none"> - Head of pancreas cancer impinges on common bile duct, resulting in obstructive jaundice (↑ ALP + ↑ direct bilirubin) in smoker with weight loss, or in patient who had gallbladder taken out years ago (so it clearly can’t be due to a stone in common bile duct). - Patient will not be febrile; can have dull abdominal pain. - Courvoisier sign is a painless, palpable gallbladder in an afebrile patient who’s jaundiced. This is pancreatic cancer until proven otherwise and is pass-level.

	<ul style="list-style-type: none"> - Pancreatic enzymes are normal in pancreatic cancer. - USMLE wants CT of the abdomen to diagnose. - Whipple procedure is done to remove head of pancreas. If the cancer is isolated to the tail, distal pancreatectomy is the answer. - Patients with pancreatectomy need pancreatic enzyme supplementation. The exam can write this as "pancrelipase."
Cholangiocarcinoma	<ul style="list-style-type: none"> - Bile duct cancer. Answer on USMLE if the vignette sounds like pancreatic cancer but they tell you in the last line CT is negative. - Answer is ERCP as next best step. - Smoking is risk factor, same as pancreatic cancer. - Can be caused by <i>Clonorchis sinensis</i> (trematode).
Cholelithiasis	<ul style="list-style-type: none"> - Stones in the gallbladder. - Presents with biliary colic, which is acute-onset waxing/waning spasm-like pain in the epigastrium or RUQ. - Pain is due to cholecystokinin causing gall bladder contractions, where a stone within the gallbladder transiently obstructs flow of bile into cystic duct. They ask this on 2CK as well, where patient will biliary colic and answer is "obstruction of cystic duct opening by stone." Not dramatic. - Classic demographic is 4Fs = Fat, Forties, Female, Fertile for cholesterol stones. This is because estrogen upregulates HMG-CoA reductase, causing ↑ cholesterol synthesis and secretion into bile. NBME will give you standard vignette of 4Fs, and then the answer will just be "increased secretion of cholesterol into bile." - Another NBME Q gives vignette of cholelithiasis, and then rather than asking for the diagnosis, they ask what the patient most likely has → answer = "lithogenic bile." Slightly awkward, but means promoting the formation of stones. - ↑ cholesterol stones in pregnancy not just due to estrogen effect but also because progesterone slows biliary peristalsis (biliary sludging). Tangentially, progesterone also slows ureteral peristalsis, which is why there's ↑ risk of pyelonephritis (as discussed in the HY Renal PDF). - Cholesterol stones most common, but pigment (calcium bilirubinate) stones are exceedingly HY for hereditary spherocytosis and sickle cell, due to ↑ RBC turnover. - USMLE wants you to know that splenectomy is Tx for hereditary spherocytosis to ↓ incidence of cholelithiasis. Sometimes the vignette wants "cholecystectomy + splenectomy" as combined Tx. Or if they say this was in a parent's Hx in patient with low Hb, you know the Dx is hereditary spherocytosis (autosomal dominant). - Infections can also sometimes cause pigment stones, but LY. - Diagnose with abdominal ultrasound. - Ursodeoxycholic acid (ursodiol) ↓ secretion of cholesterol into bile. USMLE just wants you to know this MOA + that it can be used in patients with asymptomatic cholelithiasis, those declining cholecystectomy, and in pregnancy.
Cholecystitis	<ul style="list-style-type: none"> - Cholelithiasis + fever. - Vignette will sound exactly like cholelithiasis, but if we add a fever on top of it, we now just call it cholecystitis. - Virtually always due to obstruction by a stone + infection as a result. - Diagnose with abdominal ultrasound, showing the stones. - If ultrasound is negative, do a HIDA scan. - Tx is cholecystectomy. - Emphysematous cholecystitis is air visualized within the biliary wall. USMLE wants <i>Clostridium perfringens</i> as the organism (can cause gas gangrene anywhere) in this case.

	<ul style="list-style-type: none"> - Chronic cholecystitis is calcification of the gallbladder (aka chronic calculous cholecystitis, or “porcelain gallbladder”). It is due to repeated bouts of acute cholecystitis. - ALP and bilirubin will not be increased 19/20 questions. This is because inflammation of the gallbladder doesn’t mean we have any form of common bile duct obstruction. However there is one nonsense Q on a 2CK NBME where 4 of the answers are wildly wrong, with correct answer being cholecystitis in setting of high ALP + direct bilirubin. Since cholecystitis is caused by stones virtually always, the implication is patients can occasionally have concurrent choledocholithiasis.
Choledocholithiasis	<ul style="list-style-type: none"> - Stone anywhere within the biliary tree. Don’t confuse with cholelithiasis. - Obstructive jaundice (\uparrow ALP + \uparrow direct bilirubin) in patient who has Hx of cholelithiasis or Hx of cholecystectomy performed within the past week. - Regarding the latter, the Q can say patient had cholecystectomy performed a week ago + “intra-operative cholangiography was not performed.” The implication is bile duct patency is supposed to be visualized during cholecystectomy to ensure there isn’t a stone retained within the biliary tree. However, the Q need not say “intra-operative cholangiography was not performed.” This makes the Q pass-level. - USMLE wants abdominal ultrasound followed by ERCP as the answer. ERCP tends to show up as what they want, but there is a Q floating around somewhere that asks for ultrasound first, so know that sequence. - As I talked about earlier, I’ve never seen MRCP as a correct answer. - Being able to discern choledocholithiasis from pancreatic cancer is vital for USMLE. If they give you obstructive jaundice but say the patient is a heavy smoker with weight loss, or hasn’t had a gallbladder for 25 years, you know it’s head of pancreas cancer, not choledocholithiasis. And then, once again, if it sounds like pancreatic cancer but the CT is negative, that’s cholangiocarcinoma and we do ERCP.
Gallstone pancreatitis	<ul style="list-style-type: none"> - Gallstone pancreatitis is a type of choledocholithiasis in which the stone has descended distally enough in the common bile duct that it now obstructs the hepatopancreatic ampulla. This results in a backflow of pancreatic enzymes to the pancreas causing damage \rightarrow acute pancreatitis. - USMLE wants “hepatopancreatic ampulla” as correct over “common bile duct” if they ask you to choose location of the obstruction. Slightly odd, since the stone is still in the common bile duct, but hepatopancreatic ampulla blockage is <i>why</i> we have the pancreatitis. - Vignette will give obstructive jaundice <i>but also high pancreatic enzymes</i>. - In other words, the Q will give \uparrow ALP, \uparrow direct bilirubin, and \uparrow amylase / lipase. - I repeat that pancreatic cancer will never have elevated enzymes on USMLE, so this is a pass-level means to distinguish. - New 2CK NBME has CT of the abdomen as done first, prior to ERCP. This is because even though we have a stone requiring removal from the biliary tree, CT of the abdomen first looks for pancreatic fluid collection.
Cholangitis	<ul style="list-style-type: none"> - Inflammation of the bile ducts. You must know Charcot triad for cholangitis: 1) fever, 2) jaundice, 3) abdominal pain. We classically learn this as “RUQ/epigastric pain,” but I can tell you USMLE doesn’t give a fuck and will just say “abdominal pain.” I’ve had students get cholangitis Qs wrong because they’re like, “I thought it had to be RUQ pain though.” And I’m like, yeah, I agree, but USMLE doesn’t give a fuck. - Will present 3 ways on USMLE: - 2/5 Qs will be ascending cholangitis, which is infection from ascension of bowel flora (<i>E. coli</i>, <i>Bacteroides</i>) up the common bile duct. - 2/5 Qs will be primary sclerosing cholangitis, which is inflammation of the bile ducts in the setting of IBD (always due to ulcerative colitis on USMLE,

	<p>but can rarely be due to Crohn in real life). p-ANCA can be positive, and there can be a beaded appearance of the common bile duct on cholangiogram. On 2CK NBME 10, there is a Q on primary sclerosing cholangitis where the patient is afebrile (rare; i.e., we don't have full Charcot triad), but they say patient has UC + obstructive jaundice + ERCP shows "narrowing of the bile ducts," so the answer is evidently PSC.</p> <ul style="list-style-type: none"> - 1/5 Qs will just give you a patient with history of cholelithiasis, where the implication is a stone has descended causing choledocholithiasis, which in turn led to obstruction + inflammation of the common bile duct. - USMLE wants antibiotics + ERCP to diagnose and treat. Biliary drainage by ERCP ↓ morbidity and mortality.
Acute pancreatitis	<ul style="list-style-type: none"> - ↑ amylase and/or lipase in patient who has abdominal pain. - Pain need not radiate to the back. - Alcoholism and stones are two biggest risk factors. - Hyperlipidemia and hypercalcemia can also occasionally be causes. - Can be caused by drugs (didanosine is HIV NRTI; exenatide is a GLP-1 analogue for diabetes). - Scorpion sting and mumps as causes are nonexistent on USMLE. - Can be caused by choledocholithiasis (gallstone pancreatitis; ↑ pancreatic enzymes in setting of ↑ ALP and ↑ direct bilirubin). - Results in enzymatic fat necrosis. - You don't need to memorize Ranson criteria (elaborate criteria for Surg to determine prognosis in pancreatitis). What you need to know are two main points: <ul style="list-style-type: none"> 1) ↓ Serum calcium and ↑ glucose are bad prognostic indicators. In fact, I'd say low calcium is quite possibly the highest yield variable on USMLE for pancreatitis. There are many long/vague pancreatitis Qs out there, where they'll mention ↓ calcium in the stem, and you're like "Boom pancreatitis." 2) The degree of lipase and/or amylase elevation doesn't correlate with prognosis. In other words, if amylase is 1200 versus 10,000, that's not important for patient outcome. 3) The rest of the Ranson criteria is more Surg rotation masturbation info and otherwise nonsense for USMLE. <ul style="list-style-type: none"> - It's to my observation NBME Qs will sometimes list high amylase without mentioning lipase for whatever reason. Lipase is more specific for pancreatitis, but it's what NBME sometimes does, so don't be confused. - HY initial management for 2CK is a triad: 1) NPO (nil per os; or nothing by mouth; this can be written as simply bowel rest as NBME answer); 2) NG tube decompression; 3) IV fluids with normal saline. This triad is not specific for pancreatitis, and can be done for a number of GI-related conditions, including cholangitis and stones. But it just tends to get tested a lot for pancreatitis. - After this initial triad, "CT scan of the abdomen" is answer on NBME as next best step to look for any degree of fluid collection. If a pancreatic pseudocyst is present, NBME answer is to drain this by ERCP. - It's to my observation USMLE doesn't assess antibiotics as part of pancreatitis Tx, but apparently the carbapenems (like imipenem) have fantastic penetration of pancreatic tissue.

	 <ul style="list-style-type: none"> - A 2CK NBME Q gives pancreatitis + similar image as above, and the answer is just ERCP (for drainage of the pseudocyst within black circle). - A necrosectomy is removal of pancreatic tissue in the setting of high fraction of necrosis. Patients with pancreatectomy require enzyme replacement (pancrelipase). - Acute pancreatitis is HY cause of ARDS.
Chronic pancreatitis	<ul style="list-style-type: none"> - Steatorrhea in alcoholic or patient with recurrent acute pancreatitis episodes → results in pancreatic burnout with ↓ production of pancreatic enzymes → ↓ proteases/lipases → malabsorption. - In other words, we have normal pancreatic enzymes – i.e., they are not elevated. - Question can say alcoholic has ↑ fat and protein seen in stool. - D-xylose test is normal. This is a monosaccharide that is readily absorbed by the small bowel insofar as the intestinal lining is intact. So if we get steatorrhea + normal D-xylose, this can be due to pancreatic insufficiency or lactose intolerance. If D-xylose test is abnormal, we know the malabsorption is due to an intestinal lining issue, such as Celiac or Crohn. - If the USMLE gives you a CT for chronic pancreatitis, they will show you calcification within the pancreas.  <ul style="list-style-type: none"> - Tx = pancreatic enzyme supplementation (pancrelipase).
Bile duct leak	<ul style="list-style-type: none"> - The answer on 2CK Surg if they give you patient with cholecystectomy within the past week who now has fever, abdominal pain, and ↑ direct bilirubin.

	<ul style="list-style-type: none"> - During the surgical anastomoses created during cholecystectomy, sometimes there can be a post-op bile leak, literally. Weird diagnosis but it shows up on occasion.
Sphincter of Oddi dysfunction	<ul style="list-style-type: none"> - The answer on USMLE if the Q sounds like gallstone pancreatitis (i.e., \uparrow ALP, \uparrow direct bilirubin, \uparrow pancreatic enzymes) but the patient hasn't had a gallbladder for many years (so it can't be a stone causing the obstruction).
Gallstone ileus	<ul style="list-style-type: none"> - Gallstone enters small bowel and causes an intestinal obstruction. - The answer on USMLE if they say "air in the biliary tree" (pneumobilia). - Can be caused by cholecystoduodenal fistula, which is when a patient with cholelithiasis can develop a conduit between the gallbladder and small bowel. - What the USMLE will do is give you a long, rambling paragraph where they say "air in the biliary tree" in the last line. The answer will then just be "gallstone ileus" straight up, or it will be "cholecystoduodenal fistula."
Choledochal cyst	<ul style="list-style-type: none"> - Asked on 2CK Surg. What they're going to do is give you a long, nonsense paragraph with \uparrow ALP and \uparrow direct bilirubin + they say "CT shows a cystic structure within the biliary tree." Answer = "simple excision of the cyst." Students are huh, what's going on here? \rightarrow choledochal cyst. You have to just excise it. Bullshit/dumb diagnosis. Take it up with NBME not me.
Primary biliary cirrhosis	<ul style="list-style-type: none"> - As mentioned earlier, this will be a woman 20s-50s who has generalized pruritis, \uparrow cholesterol, \uparrow ALP, \uparrow direct bilirubin, and Hx of autoimmune disease in her or a relative. - Diagnose with anti-mitochondrial antibodies as first step, followed by liver biopsy to confirm. - Initial Tx = ursodeoxycholic acid (ursodiol).
Spontaneous bacterial peritonitis (SBP)	<ul style="list-style-type: none"> - One of the highest yield diagnoses on 2CK. - Bacterial infection of peritoneal fluid by mixed enteric flora. - The answer on USMLE when they give you diffuse abdominal pain and fever in one of the three following scenarios: 1) cirrhosis; 2) recent peritoneal dialysis; 3) nephrotic syndrome. - Shifting dullness" or a "fluid wave" are buzzy for ascites, but questions will often omit these descriptors from stems. What they care about is you identifying when a patient either has a major risk factor for ascites, or are aware of a peritoneal intervention as the cause for the presentation. - In other words, they can tell you a patient has cirrhosis + abdo pain + fever, where they don't have to mention a fluid wave, but you just have to infer, "Well he/she clearly has major risk factor for ascites, so this sounds like SBP." - There is a 2CK Q where they say kid with minimal change disease (nephrotic syndrome) has abdo pain + fever \rightarrow answer = spontaneous bacterial peritonitis. - Next best step in diagnosis is abdominal paracentesis. This refers to aspiration of fluid from the peritoneal cavity. Do not confuse this with pericardiocentesis. "Paracentesis" as an answer shows up everywhere, and I've seen students avoid it because they're like, "What? I thought that meant pericardiocentesis." - After the paracentesis is done, USMLE wants a very specific order for what to do next. Choose "white cell count and differential" first if it's listed, followed by "gram stain and culture of the fluid." - This order is important because "gram stain and culture of the fluid" is a correct answer in one Q but wrong answer in another Q, where "white cell count and differential" is correct to do first. - The reason white cell count and differential is done first is because SBP is diagnosed when paracentesis shows >250 WBCs/μL. - There is a new 2CK Q where they give ascites in patient with cirrhosis, but do not mention fever or abdominal pain. However, they say paracentesis

	shows 900 WBC// μ L \rightarrow answer = "antibiotic therapy." It should be made clear though that ~6/7 SBP Qs will give abdo pain and fever. - Treatment is ceftriaxone.
Focal nodular hyperplasia	- Obscure diagnosis where they tell you adult has an abdominal CT for unrelated reason and has a 1-2-cm hepatic lesion with a central scar . There will be zero mention of trauma or infection. Every student says WTF. - This is a lesion of hepatocellular hyperplasia that does not require treatment . This is the answer on NBME, where they tell you CT shows hepatic lesion with central scar. Answer = "no further diagnostic studies indicated."

HY cirrhosis points

- Cirrhosis is a small, shrunken, burnt out liver due to chronic disease.
- HY causes are alcoholism, HepB/C, Wilson disease, hemochromatosis, NASH, α 1-antitrypsin deficiency etc.
- "Burned out" means LFTs are normal or low – i.e., there is not transaminitis as with acute hepatitis.
- **USMLE likes \uparrow PT and \downarrow clotting factor synthesis** in cirrhotic patients.
- Hyperammonemia occurs due to \downarrow urea cycle activity (normally occurs in liver). This can cause hepatic encephalopathy (confusion) and asterixis ("hepatic flap" of the hands).
- USMLE likes acute exacerbations of hyperammonemia caused by **GI bleeds** \rightarrow \uparrow ammonia absorption.
- Spontaneous bacterial peritonitis (SBP) is $\uparrow\uparrow$ HY on 2CK, as discussed above.
- Esophageal varices from \uparrow portal pressure that backs up to **left gastric vein** (discussed earlier).
- Caput medusae are visible periumbilical veins (superior epigastric veins).

Systemic inflammatory response syndrome (SIRS)

- Knowing this short table is vital for understanding many IM (and Surg) Qs on 2CK.
- In the setting of stress (i.e., due to trauma, surgery, autoimmune flare, infection), catecholamines and \uparrow sympathetic activity might shift the patient's vitals out of the normal range.
- The reason knowing SIRS is important is because the patient can have abnormal vitals **without** having an infection.

SIRS	- 2 or more of the following: - Temperature $<36^{\circ}\text{C}$ or $>38^{\circ}\text{C}$ ($<96.8^{\circ}\text{F}$ or $>100.4^{\circ}\text{F}$). - HR >90 . - RR >20 . - WBCs $<4,000$ or $>12,000$.
Sepsis	- SIRS + source of infection.
Septic shock	- Sepsis + low BP.
<ul style="list-style-type: none"> - Sometimes you will see a patient's vitals slightly out of the normal range in the setting of trauma, surgery, or autoimmune flares, and you have to be able to say, "There's no infection. That's just SIRS from sympathetic activation." - Knowing if a patient is septic is important for management of patients on 2CK, where sometimes antibiotic regimens are stepped up. For example, when treating PID, if the patient is septic, intravenous ceftriaxone and azithromycin is correct on one of the 2CK NBMEs; IM ceftriaxone and oral azithromycin is wrong. This is because the latter is for most patients who have PID but aren't septic. - Ceftriaxone is frequently an answer on 2CK for in-hospital patients who are septic from a variety of community-acquired conditions, e.g., pneumonia, pyelonephritis, prostatitis. For instance, community-acquired pneumonia is empirically treated with azithromycin (on 2CK NBME 8), but if patient is septic, we can go straight to ceftriaxone (have seen this more than once on 2CK NBMEs). - For hospital-acquired infections in which patients are septic, NBME goes hard-hitting with vancomycin PLUS ceftazidime or cefepime. This regimen covers MRSA and <i>Pseudomonas</i>. 	

HY Referred pain	
Spleen	- Splenic laceration → ULQ pain +/- can refer to left shoulder (Kehr sign).
Diaphragm	- Diaphragmatic irritation can cause pain going to left shoulder (asked on NBME); spleen is wrong answer. The key here is they ask "irritation."
Gallbladder	- RUQ or epigastric pain +/- can refer to right shoulder.
Appendix	- Epigastric pain initially (visceral peritoneal inflammation) that migrates to RLQ (parietal peritoneal inflammation).

HY GI Diagnostic modalities for IM	
- Same as with the GI surgeries table above, we could discuss endless indications for the below modalities, but I'm staying concise here with just the highest yield points.	
Nasogastric tube	- "Insertion of NG tube" is the answer for tracheoesophageal fistula and choanal atresia (discussed in HY Pulm PDF).
Barium swallow	- For suspected Zenker; shows outpouching. - First step in achalasia (before manometry); shows bird's beak. - Do not use for esophageal perforation. Can cause mediastinitis if it leaks out through a hole in the esophagus. - Can be used for patients with aspiration risk, since it doesn't cause pneumonitis.
Gastrografin swallow	- Aka water-soluble contrast swallow. - Used for esophageal perforations because it doesn't cause mediastinitis. - Do not use if patient has aspiration risk; causes pneumonitis. Use barium instead.
Esophageal manometry	- Answer for achalasia after barium swallow shows bird's beak. - A pressure study of the esophagus.
Endoscopy	- Aka esophagogastroduodenoscopy. - Immediate answer for any patient with new-onset dysphagia and Hx of GERD or heavy smoking/alcohol (for esophageal cancer). Then biopsy any lesion/stricture. - Endoscopy + banding for esophageal varices emergent management. - Diagnosis of hiatal hernia (asked on NBME). - Done in patients over 50 who have <i>H. pylori</i> positivity (on newer 2CK form).
Capsule endoscopy	- Always wrong fucking answer on USMLE.
Upper GI series	- Congenital midgut volvulus in pediatrics; will show a corkscrew. - This is a contrast swallow followed by X-rays to visualize the upper GI tract.
Abdominal ultrasound	- Cholelithiasis. - First step to diagnose cholecystitis; if negative, do HIDA scan. - First step for choledocholithiasis, then do ERCP. - Intussusception Dx, then do enema (definitively diagnostic and therapeutic). - Pyloric stenosis.
HIDA scan	- Answer for confirmatory diagnosis of cholecystitis (not cholelithiasis alone) if ultrasound is negative. - Radiocontrast is injected + secreted into bile. If gallbladder lights up, there is no obstruction of the cystic duct and it is negative; if gallbladder doesn't light up, we know there's an obstruction by a stone and it confirms cholecystitis.
CT of abdomen	- USMLE won't force you to choose, but just assume contrast CT is always used. The only times non-contrast CT will be an answer is for urolithiasis and intracranial bleeds. - Diagnosis of pancreatic cancer (highest yield indication on USMLE). - Diagnosis of liver cancer and focal nodular hyperplasia. - Renal injury (ultra-HY; discussed in HY Renal PDF). - Blunt force trauma to abdomen in patient who is stable. - Diverticulitis.
Abdominal x-ray	- Used to look for bowel gas in suspected obstruction (e.g., sigmoid volvulus showing coffee bean sign). - Duodenal atresia (double-bubble sign).

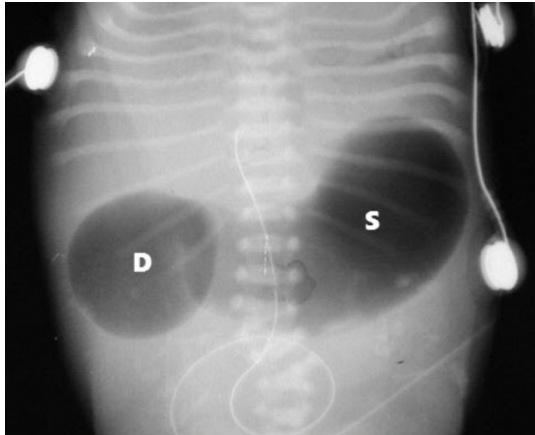
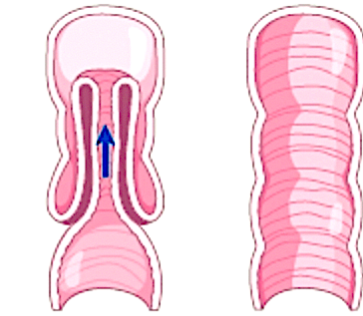
	<ul style="list-style-type: none"> - Congenital diaphragmatic hernia (bowel gas in left hemithorax). - Necrotizing enterocolitis (pneumatosis intestinalis). - Toxic megacolon if patient is stable. - "X-rays of chest and abdomen" used for duodenal ulcer perforation to look for air under the diaphragm.
ERCP	<ul style="list-style-type: none"> - Endoscopic retrograde cholangiopancreatography; type of EGD that can also enter the biliary tree, remove stones there, and inject contrast if necessary. - Answer on USMLE for choledocholithiasis (including gallstone pancreatitis) after ultrasound is performed. - Answer for diagnosis of cholangitis. - Answer for drainage of pancreatic pseudocyst.
MRCP	<ul style="list-style-type: none"> - Magnetic resonance cholangiopancreatography. - Never seen this as correct answer on NBME, but I observe that students always pick it when they don't know what's going on, maybe because it sounds weird and specific. - Can visualize biliary tree much more safely than ERCP, but unlike ERCP, it isn't a form of treatment (ERCP is both diagnostic and therapeutic).
Endoscopic ultrasound	<ul style="list-style-type: none"> - Never seen this as correct answer, only wrong answer. - Can be done to diagnose pancreatic cancer if CT is negative or to drain pancreatic fluid collections in place of ERCP. But once again, never seen this as correct.
Paracentesis	<ul style="list-style-type: none"> - Used for spontaneous bacterial peritonitis. - As mentioned earlier, choose "white cell count and differential" before "gram stain and culture of the fluid." Do not confuse with pericardiocentesis.
Meckel scan	<ul style="list-style-type: none"> - Radiocontrast uptake scan that localizes to the diverticulum at terminal ileum.
Colonoscopy	<ul style="list-style-type: none"> - Done for diagnosis of colorectal cancer, IBD, pseudomembranous colitis. - Do not do in diverticulitis (can cause perforation; do CT instead). - Do if patient has anal cancer prior to excision in order to first see if there's greater extent of cancer (might change management). Asked on 2CK form, where they say there is cancer at anal verge, and excision is wrong; answer is colonoscopy. - Commence at age 45-50 (guidelines are evolving) and then do every 10 years. - USMLE will not force you into a position where ohemgee is it 45 or 50. If they force you to choose 45 as a new guideline, it will be obvious the other answer choices are wrong. - If first-degree relative (parent or sibling) has colon cancer, commence at age 40 or 10 years prior to diagnosis in that family member, whichever is earlier. In other words, never later than 40. For example, if dad was diagnosed at 58, commence at age 40. If dad was diagnosed at 44, commence at age 34. Then do every 5 years. - If patient has IBD (UC or Crohn), commence 8 years after the diagnosis was made and then do every 2-3 years. 2CK NBME is real slick about this. They give mid-30s patient with IBD diagnosed in 20s + also has dad diagnosed with colon cancer in 50s; wrong answer = colonoscopy at age 40; correct answer is "colonoscopy now," since patient has IBD and should have had one done 8 years after his/her diagnosis. - Patients who have history of dysplastic polyps need repeat colonoscopies every 2-5 years, depending on size/morphology of polyp(s). - If patient has HNPCC (Lynch syndrome), start at 20-25, then do every 1-2 years. - For FAP, start at age 10-12 and do every 1-2 years. Then do prophylactic proctocolectomy at age 18 (on NBME). - For Peutz-Jeghers, start at age 8, then every 1-2 years.
Sigmoidoscopy	<ul style="list-style-type: none"> - "Sigmoidoscopy-guided insertion of rectal tube" is answer on NBME for treatment of sigmoid volvulus.

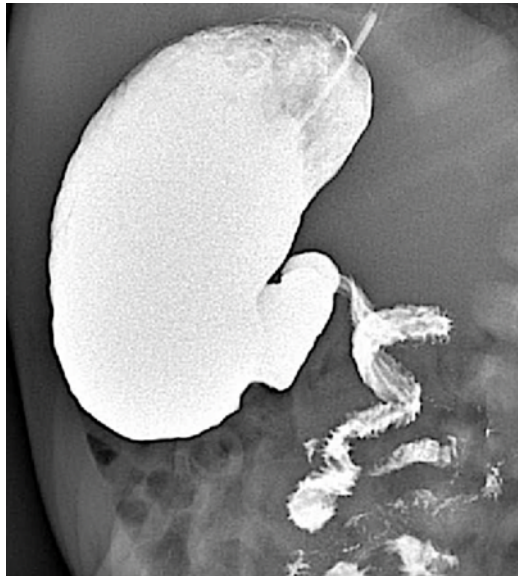
	- I've never seen sigmoidoscopy as a diagnostic tool. I make this point because there are alternative theoretic regimens to colon cancer screening – i.e., sigmoidoscopy + barium enemas, etc., but I've never seen these assessed.
Anoscopy	- Shows up on newer 2CK form as answer for diagnosis of hemorrhoids before banding is performed. This will help determine extent of hemorrhoids.

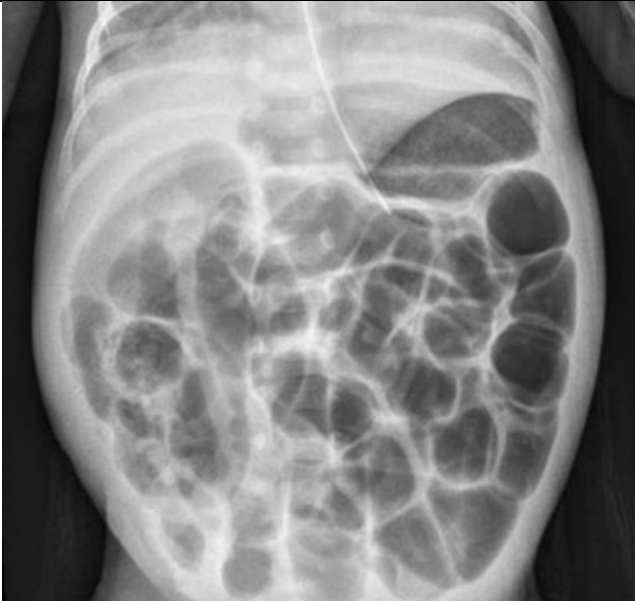
HY Polyp conditions for USMLE	
Lynch syndrome	<ul style="list-style-type: none"> - Hereditary non-polyposis colorectal cancer (HNPCC). - Mismatch repair genes <i>MSH2/6</i>, <i>MLH1</i>, <i>PMS2</i>. - Mutations cause "microsatellite instability." - Colonic polyps/cancer; also associated with gynecologic cancer. - Start colonoscopy at age 20-25, then do every 1-2 years.
Familial adenomatous polyposis	<ul style="list-style-type: none"> - Familial Adenomatous Polyposis (FAP); chromosome 5; AD. - Hundreds to thousands of polyps on colonoscopy; 100% cancer risk. - Start colonoscopy at age 10-12 and do every 1-2 years. Then do prophylactic proctocolectomy at age 18 (on NBME). - FAP + soft tissue (e.g., lipoma) or bone tumors (e.g., of the skull) = Gardner syndrome. - FAP + CNS tumors = Turcot syndrome.
Peutz-Jeghers	<ul style="list-style-type: none"> - As talked about at the start of this PDF, this is combo of perioral melanosis and hamartomatous colonic polyps. - Start colonoscopy at age 8, then do every 1-2 years.
Juvenile polyposis	<ul style="list-style-type: none"> - Shows up on a 2CK NBME. - Q will tell you there's a teenager (i.e., juvenile, LOL!) with intermittent bleeding per rectum + colonoscopy shows scattered polyps + biopsy shows "dilated, cystic, mucus-filled glands with abundant lamina propria and inflammatory infiltrates" → answer = juvenile polyposis. - Only question I've seen on it, but it's on new 2CK NBME so I have to mention it.
Hyperplastic polyps	- All you need to know is these are not pre-cancerous / have no dysplasia .
Tubulovillous	<ul style="list-style-type: none"> - Dysplastic polyps that precede full-blown colorectal cancer are classically either tubular or villous, AND either pedunculated or sessile. - Villous is worse than tubular. Sessile is worse than pedunculated. - This means pedunculated tubular polyps are "best" and sessile, villous polyps are "worst." - Sessile means flat; pedunculated means "sticks out." - Polyps can have mixed characteristics and hence be tubulovillous. - What you need to know is: USMLE will give you a random 65-year-old with a polyp + show you a pic + ask you what it is → answer = "tubular polyp." Student freaks out and says, "Wait, we need to know polyp pics??" → No. The big picture concept is that older people who get colorectal cancer will have tubular, villous, or tubulovillous polyps as I just said. Wrong answers would be things like hamartomatous, juvenile, and hyperplastic. You can just eliminate to get there without even knowing the image. - 2CK wants you to know that patients with history of dysplastic polyps need repeat colonoscopies every 2-5 years, depending on size/morphology of polyp(s).

Colon cancer short points
<ul style="list-style-type: none"> - <i>KRAS</i> gene is the answer on USMLE for the first gene mutated in colonic polyps, prior to progression to overt colon cancer. - Colon cancer often develops as a result of <i>progressive</i> mutations, rather than one mutation straight-up. In other words, first <i>KRAS</i>, then <i>PTEN</i>, then <i>DCC</i>, then <i>TP53</i>.

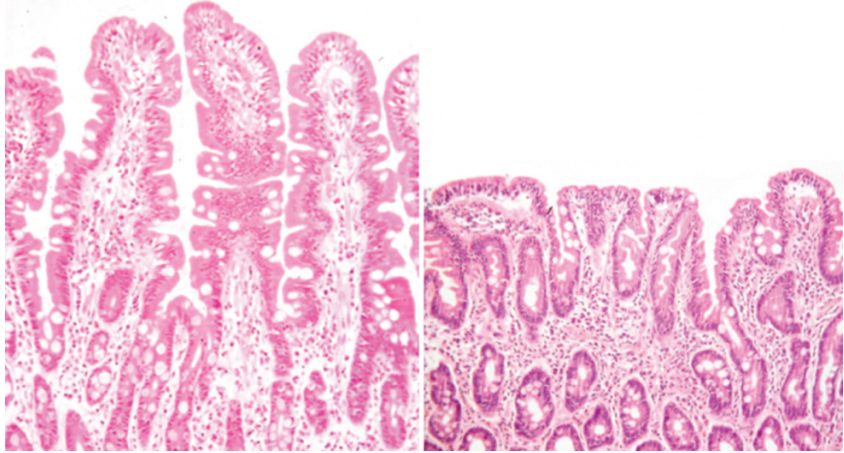
- If they tell you a colon cancer has metastasized and force you to choose a gene that's mutated, go with *TP53* for p53 protein.
- If they tell you a polyp is seen and there is no evidence of invasion of the stalk, choose *KRAS*. This reflects earlier changes in the sequence as I just wrote above.
- Can cause **colovesicular** fistulas, where a passageway develops between the GI tract and bladder, leading to UTIs and mixed enteric flora in the urine. This is also assessed for diverticulosis on 2CK and seems to be a new diagnosis USMLE likes. This could also be due to Crohn, in theory, but I haven't seen it on NBMEs yet.
- Can cause *Strep bovis* endocarditis. Obscure, but rare point assessed on USMLE.
- I already discussed colon cancer screening extensively above.


HY Peds GI DDx	
Pyloric stenosis	<ul style="list-style-type: none"> - Forceful/projectile non-bilious vomiting in neonate days to weeks old. Obstruction is above level of duodenum, so we won't see bile. - Students fixate on exact age of the kid for pyloric stenosis versus duodenal atresia. USMLE doesn't give a fuck and will give variable ages. - Hypertrophic pylorus; "olive-shape mass" in abdomen is buzzy but rarely seen in Qs. - Ultrasound done to diagnose; myotomy to treat. - USMLE wants you to know this is almost always a one-off / sporadic developmental defect, where the neonate will not have a broader syndrome. In contrast, duodenal atresia is usually Down syndrome.
Duodenal atresia	<ul style="list-style-type: none"> - Bilious vomiting in neonate. Bilious = obstruction at level of duodenum or lower. - Associated with Down syndrome, albeit not mandatory. - Will cause double-bubble sign on abdominal x-ray. 
Annular pancreas	<ul style="list-style-type: none"> - Another cause of duodenal obstruction with double-bubble sign, but much more rare than duodenal atresia.
Intussusception	<ul style="list-style-type: none"> - Intussusception is telescoping of the bowel into itself.  <p style="text-align: center;">Intussusception Normal</p> <ul style="list-style-type: none"> - Almost always under age 2.

	<ul style="list-style-type: none"> - Idiopathic, but can be triggered by viral infection or rotavirus vaccination, where mesenteric lymphadenopathy can act as a “lead point” for the intestinal telescoping. Underlying Meckel diverticulum is also a common lead point. - In ultra-rare scenarios, intussusception in elderly can occur due to colon cancer. - Classic presentation is intermittent/colicky abdominal pain, where the kid will have episodes of drawing the legs to the chest or squatting, with blood in the stool +/- bilious vomiting. - An abdominal mass (i.e., sausage-shaped mass) is a key feature, but not in all Qs. - Diagnosis is first done with ultrasound, which may show a sausage mass or target sign (I’ve never seen NBME show the image, so they don’t care). After the ultrasound, enema is both diagnostic and therapeutic. USMLE doesn’t care what kind of enema is used; air-contrast enema is classic, but you will see all different types of enemas as correct answers. - “Air enema with ultrasound” is the answer on one 2CK form.
Midgut volvulus	<ul style="list-style-type: none"> - Failure of rotation of proximal bowel. - Almost always under age 1. - Presents similarly to intussusception (often mistaken for it), but there is no mass. - Upper-GI series shows corkscrew appearance.  <p>The image is a black and white fluoroscopic upper gastrointestinal (GI) series. It shows a large, dilated, and coiled loop of the small intestine, which has a characteristic 'corkscrew' or 'beak-like' appearance. This is a classic radiographic sign of midgut volvulus, where the midgut has rotated around its mesenteric axis, leading to obstruction and potential ischemia.</p> <ul style="list-style-type: none"> - If an abdominal x-ray is performed, it will show “dilated loops of small bowel with air fluid levels,” since we have an obstruction. - Treatment is surgical.
Necrotizing enterocolitis	<ul style="list-style-type: none"> - Necrotic bowel occurring in premature neonates born <32 weeks’ gestation. - Presents with pneumatosis intestinalis (air in bowel wall); resembles bubbles.

	 <ul style="list-style-type: none"> - USMLE will show you above image in kid born, e.g., at 26 weeks' gestation, and then answer is just necrotizing enterocolitis. Not hard. - It's to my observation necrotizing enterocolitis usually shows up as a <i>wrong</i> answer choice on NBMEs, where I see students pick it in, e.g., an adult, and I'm like, "Dude you see that in fucking hyper-preemies." And they're like Oh. So you need to remember this as specifically a premature neonate condition.
Hirschsprung	<ul style="list-style-type: none"> - Failure of migration of neural crest cells distally within the colon. - Causes an aganglionic distal segment that results in \uparrow anal sphincter tone. <div data-bbox="477 1128 1339 1653"> <p>Normal</p> <p>Hirschsprung's disease</p> <p>Ganglion cells</p> <p>No ganglion cells - area affected by Hirschsprung's</p> </div> <ul style="list-style-type: none"> - Often associated with Down syndrome. - Presents usually as failure to pass stool at birth, as chronic constipation in an infant, depending on the severity. But do not confuse with "meconium ileus," which is a term that refers to failure to pass stool at birth specifically due to cystic fibrosis. - Diagnose with anal manometry showing \uparrow anal sphincter tone, followed by biopsy.
Cystic fibrosis	<ul style="list-style-type: none"> - Discussed in extensive detail in the HY Pulm PDF. - Just a reiteration that meconium ileus + exocrine pancreatic insufficiency are exceedingly HY.

	<ul style="list-style-type: none"> - Secretions within the pancreatic ducts are inspissated (meaning desiccated / dried up within a lumen), making them sticky. This means the enzymes can't make their way to the duodenum → fat-soluble vitamin malabsorption → NBME exams love vitamin E deficiency in CF in particular (presents as neuropathy). - D-xylose test is normal, since the intestinal lining/architecture is intact. Any malabsorption that occurs is due to mere paucity of enzymes in the small bowel. Recall that abnormal D-xylose test would be Celiac and Crohn on USMLE.
Biliary atresia	<ul style="list-style-type: none"> - As discussed earlier, ↑↑ direct bilirubin in a kid under the age of 6 weeks. - Caused by lack of development of the intrahepatic bile ductules and biliary tree. - Ultrasound will be done first, but USMLE wants liver biopsy to confirm the diagnosis. - Kasai procedure is done to treat, followed by liver transplant if unsuccessful.

Autoimmune intestinal absorptive disorders	
Celiac disease	<ul style="list-style-type: none"> - Intolerance to gluten (i.e., to gliadin proteins found in wheat, oats, rye, and barley; but not rice). - Causes type-IV hypersensitivity response where T cells attack the small intestinal villi, resulting in flattening of the villi and malabsorption. The biopsy/image is pass-level. Below, we have normal villi on the left, and flattening of villi in Celiac on the right.  <ul style="list-style-type: none"> - Even though the disorder is T-cell-mediated destruction of the villi, patients still develop antibodies which are HY: anti-endomysial (aka anti-gliadin) and anti-tissue transglutaminase IgA. - Patients with concurrent IgA deficiency will have false (-) results for tissue transglutaminase IgA antibody. Since "autoimmune diseases go together," and "autoimmune and immunodeficiency syndromes go together" patients with IgA deficiency have 15x greater likelihood of developing Celiac. - Celiac presents as vague bloating/diarrhea in patients who might not be able to pinpoint what they're eating to cause the symptoms. - I'd say one of the highest yield points on USMLE regarding Celiac is that it can cause iron deficiency anemia. This is because iron absorption in the duodenum is impaired from the flattened villi. - For example, you might get a difficult/vague vignette where you're not sure if the diagnosis is Celiac or lactase deficiency, but you see that hemoglobin is low, and you're like "Boom. Celiac." - Associated with dermatitis herpetiformis, which presents as itchy, vesicular lesions on extensor areas. This causes "IgA deposition at dermal papillae."

	 <ul style="list-style-type: none"> - D-xylose test is abnormal because the intestinal lining/architecture is abnormal (i.e., we have flattening of villi). - Increased risk of gastrointestinal T-cell lymphoma in Celiac. This is called enteropathy-associated T-Cell lymphoma (EATL). - Diagnosis is made via antibody screening, followed by duodenal biopsy as confirmatory. - Treatment of Celiac is simply with gluten-free diet.
Lactose intolerance	<ul style="list-style-type: none"> - Deficiency of brush border disaccharidase (i.e., aka lactase deficiency). - Brush border is located at “tips of the villi.” This is in contrast to stem cells of the GI tract, which are located at the “base of the crypts.” USMLE asks the locations of these things. - Diarrhea/bloating in response to dairy. - In contrast to Celiac disease, there is no iron deficiency anemia. - ↑ incidence in Asians, but can also develop idiopathically starting in teenage years-onward. When a young adult has a new-onset diarrhea-related condition, it’s usually lactose intolerance, as lactase production can ↓ with age. But once again, USMLE can trick you, so I’ll be an asshole and reiterate that if you see ↓ Hb, choose Celiac instead. - Secondary lactose intolerance can occur following viral gastroenteritis (e.g., rotavirus or Norwalk virus) → sloughing of the tips of villi → vignette will say new-onset diarrhea/bloating following gastro illness 1-2 weeks ago. This is only transient and patient will recover. This is HY cause of lactose intolerance. - Biopsy is normal. This is in contrast to the flattened villi in Celiac. - Diagnosis is made using hydrogen breath test or detecting ↓ stool pH. - D-xylose test is normal, since the intestinal lining/architecture is intact. - Treatment is with avoidance of lactose-containing products, or with lactase pills.
Milk protein allergy	<ul style="list-style-type: none"> - Biggest risk factor is not being exclusively breastfed for the first 6 months of life. - Will present as blood in the stool in a child who they say is, e.g., 4 months old, who was started on formula 3 weeks ago. - Treatment is switching to hydrolyzed casein formula. Switching to soy-based formula is wrong fucking answer. There is up to 50% crossover of allergy cases with kids who have milk- and soy-protein allergy. - Vignette can say kid was started on either a cow-milk or soy formula when symptoms started. It doesn’t matter. Just choose hydrolyzed casein as answer.

Inflammatory bowel disease (IBD)

- Refers to both ulcerative colitis (UC) and Crohn.
- Both can present with bloody, mucoid stools.
- Both are associated with HLA-B27 → PAIR → Psoriasis, Ankylosing spondylitis, IBD, Reactive arthritis.

- For example, if a patient has psoriasis + bloody stools, you say, "The bloody stools are probably IBD." Or likewise, if patient with known IBD has lower back pain that's worse in the morning, you say, "that's probably ankylosing spondylitis."

- Both UC and Crohn can be associated with other autoimmune diseases unrelated to HLA-B27, like vitiligo.

- Both can cause anterior uveitis (non-specific finding seen in many autoimmune diseases).

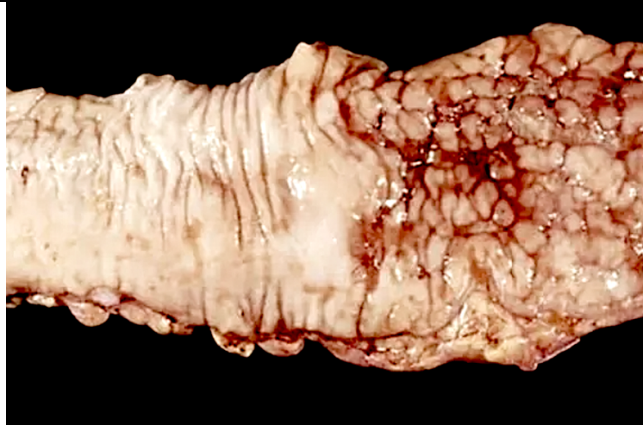
- Both have ↑ risk of colon cancer if the colon is involved. But if you're forced to choose, UC has > risk than Crohn because the colon is always involved in UC but not always in Crohn.

- Both are treated with 5-ASA NSAID compounds (**mesalamine / sulfasalazine**) or steroids. If they ask first Tx, go with mesalamine or sulfasalazine, whichever they list (they won't list both) over steroids. Q on 2CK IM form 8 has "prednisone therapy" as answer for Crohn, but a 5-ASA isn't listed.

- USMLE wants you to know anti-TNF- α agents (i.e., infliximab, adalimumab, etanercept) are used in IBD in patients who fail initial Tx with 5-ASAs and steroids.

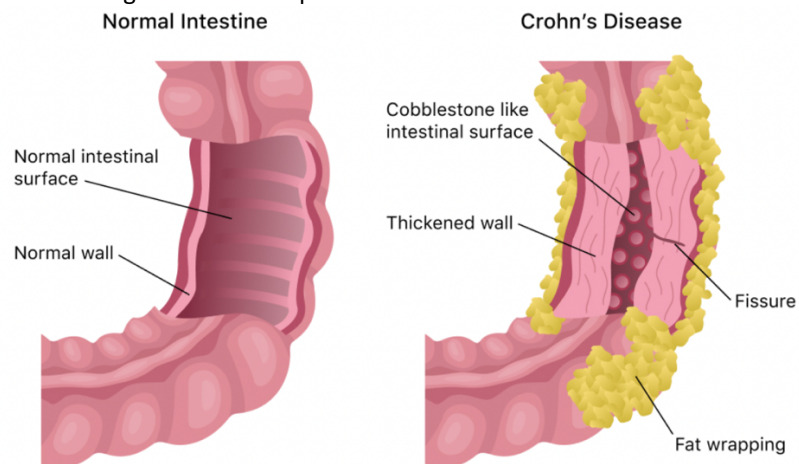
- If they ask you for which cytokine can be anti-inflammatory for IBD, the answer is IL-10. Sounds weird, but just know IL-10 and TGF- β are mostly anti-inflammatory mediators. Don't worry about Th1 vs Th2 nonsense.

<p>Ulcerative colitis</p>	<ul style="list-style-type: none"> - Rectum-ascending. - Not transmural – i.e., only affects mucosa and submucosa. This means fistulae are not seen. If they say fistulae to the skin overlying the anus or to any organ, this means transmural involvement (Crohn). - Colonoscopy will show pseudopolyps and crypt abscesses. You don't need to know what these look like. You just need to know they = UC. - Barium enema shows "lead-pipe appearance" due to loss of haustra. This detail is very important for UC. <div data-bbox="691 943 1185 1357" data-label="Image"> </div> <p>Descending colon resembles a "lead pipe"</p> <ul style="list-style-type: none"> - Can cause primary sclerosing cholangitis, as discussed earlier. This can be associated with pANCA antibodies. - Pyoderma gangrenosum is a necrotic skin lesion seen rarely in patients with UC. There is an NBME Q that describes this as an "ulcer with necrotic debris." - Can cause toxic megacolon, which presents as SIRS and sometimes low BP in a patient with UC. They might say abdominal x-ray shows a 12-cm cecum (NR 3-8). - If the patient has normal BP, NBME for 2CK wants steroids first for toxic megacolon. If the patient is unstable, go straight to laparotomy. - Colectomy is sometimes performed in patients with severe UC, but very rarely in Crohn.
<p>Crohn disease</p>	<ul style="list-style-type: none"> - "Mouth to anus" – i.e., can occur anywhere in GI tract. USMLE loves giving mouth ulcers in Crohn. But terminal ileum is highest yield location. - Transmural – i.e., can cause anal fistulae + to other organs. - Colonoscopy shows skip lesions, where there is alternating diseased vs normal bowel segments, with cobblestone ulcers.

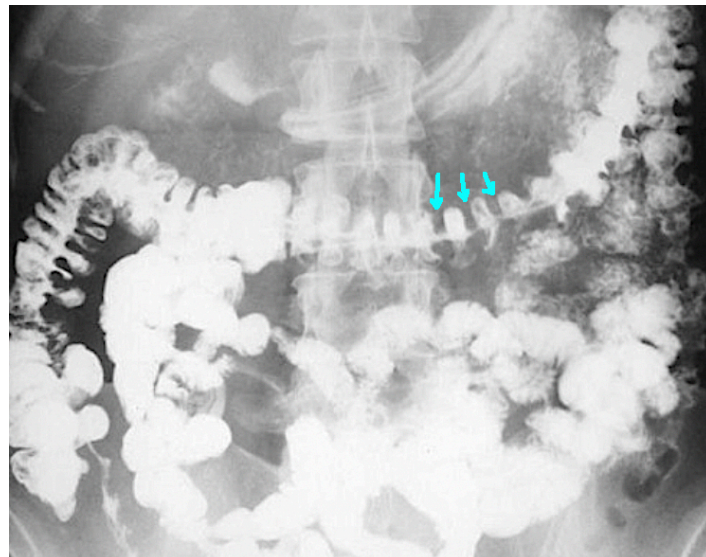


Skip lesion (left part normal + right part inflamed and cobblestoned)

- "Creeping fat" is buzzy term that can be seen on NBME, which refers to intestinal fat migration that wraps around the bowel.



- Barium enema shows "string sign," where inflamed segments are narrowed in comparison to normal bowel.



- Biopsy shows **non-caseating granulomas**. Very HY for USMLE you know that Crohn + sarcoidosis both have non-caseating granulomas.
 - Sometimes associated with erythema nodosum. Not specific for Crohn in any regard, but tends to have ↑ association, whereas UC is pyoderma gangrenosum.

	<ul style="list-style-type: none"> - Can cause anti-saccharomyces cerevisiae (yeast) antibodies. This is on a 2CK NBME, where they say (-) for these Abs, but (+) for pANCA, where answer is UC. - Intestinal malabsorption can occur, resulting in B12 deficiency most commonly due to terminal ileum being classic inflammatory location. - Impaired fat absorption can result in ↑ calcium oxalate urolithiasis, as discussed in the HY Renal PDF.
--	--

Irritable bowel syndrome (IBS)	
	<ul style="list-style-type: none"> - Don't confuse with IBD. IBS is psychosomatic (i.e., psych-related) condition. - Classic vignette will be a woman 20s-40s with stress factors who usually has alternating diarrhea / constipation; can also present as bloating or cramping. - Key detail is that symptoms are relieved with bowel motions. - NBME assesses "smooth muscle hypersensitivity" as the answer for the mechanism for IBS. - Treatment for diarrhea-predominant IBS is loperamide, which is an opioid that causes constipation. USMLE will give vignette of IBS with diarrhea, and then the answer is just "mu-opioid receptor agonist."

Other HY GI motility scenarios	
Diabetes	<ul style="list-style-type: none"> - Diabetic gastroparesis = ↓ peristalsis due to neuropathy of the GI tract. - Presents as GERD-like presentation in someone with Hx of advanced diabetes. - USMLE wants endoscopy first to rule-out physical obstruction. If endoscopy is negative, do gastric-emptying scintigraphy (aka gastric emptying scintigraphic assay) to confirm delayed gastric emptying. - Metoclopramide is used 1st for Tx. It is a prokinetic agent (i.e., ↑ peristalsis) and anti-emetic. It is a D2 antagonist but also an antagonist of serotonin 5HT3 and agonist of 5HT4 receptors. The effects on serotonin receptors ↑ gut peristalsis. - Erythromycin can also be used to agonize motilin receptors. - "2-week trial of PPI" is wrong answer. This is the answer for "regular GERD." If the patient has GERD-like presentation with advanced diabetes, however, the Dx is diabetic gastroparesis, not GERD. - Neuropathy to the hypogastric nerves (sympathetic) causes severe diarrhea. This is because the sympathetic nerves are "anti-peristalsis," so if we knock them out, we get too much peristalsis. - Neuropathy to the pelvic splanchnic nerves (parasympathetic) causes severe constipation. This is because the parasympathetic nerves are pro-peristalsis, so if we knock them out we get unopposed hypogastric. - In other words, diabetes + diarrhea → answer = hypogastric nerves are fucked up. - Diabetes + constipation → answer = pelvic splanchnic nerves are fucked up.
Thyroid	<ul style="list-style-type: none"> - Hypothyroidism can cause constipation. - Hyperthyroidism can cause diarrhea. - USMLE will give vignette of a thyroid condition with GI disturbance, and then the answer will just be "motility disorder." This is same answer for diabetes.
Supplements	<ul style="list-style-type: none"> - Iron and Aluminum can cause constipation ("Aluminum amount of feces.") - Magnesium can cause diarrhea.
Drugs	<ul style="list-style-type: none"> - Verapamil causes constipation. - Macrolides, orlistat, and α-glucosidase inhibitors (e.g., acarbose) cause diarrhea.

Viral hepatitis	
Two foundational points you need to know:	
<p>1) Hep A and E cause acute hepatitis only. Hep B, C, and D can cause chronic hepatitis.</p> <p>2) HY point is that hepatocellular damage from hepatitis is due to T-cell-mediated apoptosis, not direct viral cytopathicity. Same goes for general hepatic inflammation. Choose T cell response, not direct viral effect.</p> <p>- Hepatitis in general classically has ALT > AST, where #s can be in the hundreds to thousands, but I've seen plenty of variability on NBME Qs, which is why I don't consider this a foundational point.</p>	
Hep A	<ul style="list-style-type: none"> - The answer for acute hepatitis in the United States most of the time. The Q might say the patient had recent travel to Mexico. - Fecal-oral; only causes acute hepatitis. - IgM against HepA means acute infection. - IgG against HepA means patient has cleared infection (because there is no chronic HepA). - USMLE wants you to know HepA vaccine is indicated for IV drug users and MSM. There's a 2CK NBME Q where they just mention otherwise healthy MSM, and answer is Hep A vaccination.
Hep B	<ul style="list-style-type: none"> - Mandatory stuff for USMLE is the serology (I discuss below). - Most common hepatitis infection in the worldwide. USMLE likes China for hepatitis B. Just a pattern I've noticed. Due to ↑↑ unvaccinated. In the USA, HepC is most common. - Parenteral; can be acute or chronic. - Transmitted vertically from mother to neonate, sex, via IV drugs, or blood exposure. - Present in all body fluids, including breast milk. - Serology very HY: <ul style="list-style-type: none"> - (+) Surface antigen = patient currently has HepB. - (+) Surface antibody = patient is immune to HepB. - (+) Core antibody = patient has HepB now or did in the past. <ul style="list-style-type: none"> - (+) Core antibody IgM = patient has acute infection. - (+) Core antibody IgG = patient has chronic HepB, OR cleared HepB. - (+) Surface antibody / (-) Core antibody = Immune → Vaccinated against HepB. - (+) Surface antibody / (+) Core antibody = Immune → History of HepB / cleared it. - (-) Surface antibody / (-) Core antibody = Not immune / Susceptible → need to vaccinate. - (-) Surface antigen / (-) Surface antibody / (+) Core antibody IgM → window period (below). - Vaccination against HepB is at birth, 2 months, and 6 months (no longer at 4 months). - Only give HepB IVIG to neonate if mom is confirmed (+). A 2CK NBME Q gives mother's status as unknown when child is born → answer = "Give HepB vaccine now + only give IVIG if mother is positive." - If patient has Hx of completed HepB vaccination but has titers that show susceptibility, the answer is just "give more vaccine." Sometimes people's immunity wanes. - Once a susceptible patient is exposed to HepB and the immune system attempts to clear it, sometimes Surface antigen will decline to the point that it is no longer detectable. But at the same time, the Surface antibody might not be high enough / at detectable levels yet. This is called the "window period," where both Surface antigen and antibody are negative, so it can appear as though the patient doesn't have an infection. However, Core antibody IgM will be (+). So the key point is that 1) you know the double-negative Surface antibody/antigen combo is seen in the window period, and 2) that Core antibody IgM is most reliable during the window period. - USMLE really doesn't give a fuck about HepB pharm (i.e., entecavir, tenofovir). Waste of time. - You could be aware that interferon-α can be used for HepB.
Hep C	<ul style="list-style-type: none"> - Hepatocellular damage is due to T cells / death is due to T-cell-mediated apoptosis, not direct viral cytopathicity. I already mentioned this at top of chart, and this applies to the other Heps as well, but I reinforce this as what I'd still say is the highest yield point for HepC on USMLE. - Parenteral; can be acute or chronic.

	<ul style="list-style-type: none"> - Transmitted almost exclusively from IV drugs/blood exposure. Not present in breastmilk and non-sanguineous body fluids (in contrast to HepB). - In contrast to HepB, HepC is not considered sexually transmitted. Large longitudinal study of couples with one HepC(+) partner showed sexual transmission almost nil (possibly due to menses exposure). If you're forced to choose on NBME, however, still inform that abstinence or barrier contraception minimizes risk. - No vaccine due to ↑↑ antigenic variation (i.e., >7 genotypes and 80 subtypes of HepC exist). - IgM against HepC means acute infection. - IgG against HepC means usually means chronic HepC. - Many drugs can be used to treat. USMLE doesn't care. What you could be aware of is pegylated interferon-α.
Hep D	<ul style="list-style-type: none"> - Requires hepatitis B in order to infect, which can be due to co-infection (happening at the same time) or superinfection (occurs later in someone who already has HepB). - If USMLE asks how to prevent HepD infection, answer = vaccination against hepatitis B. There is no vaccine against HepD. - Apparently HepB antigen forms the envelope for HepD (i.e., forms a circle around HepD).
Hep E	<ul style="list-style-type: none"> - Causes fulminant hepatitis / ↑↑ risk of death in pregnant women. - Same as with HepA, only causes acute hepatitis. - Seen more in Asia, e.g., Tibet. But if USMLE says Mexico + pregnant woman + fast death from hepatitis, you still have to use your head and know that's HepE over HepA.

Other HY hepatitis causes	
NASH	<ul style="list-style-type: none"> - Answer on USMLE for liver condition in an overweight patient with normal labs. - Non-alcoholic steatohepatitis. - Underrated diagnosis in that students often have no idea about it but it shows up on both Steps (higher yield on 2CK IM). - Patient will have metabolic syndrome (i.e., ↑ BMI + ↑ lipids) + either mild transaminitis or completely normal labs. I'd say ~50% of Qs will give ALT and AST a very tiny bit elevated; the other ~50% of Qs will give you completely normal labs where you say WTF. - For example, they'll give you 40-year-old patient with BMI of 35 who comes in for routine health maintenance exam who has no complaints + lab studies are all completely normal; then the answer is just "fatty liver" or "non-alcoholic steatohepatitis." Student says, "Wait, but the labs are completely normal though." → Exactly. There's nothing wrong. But it's assumed most overweight people have some degree of fatty liver. - The condition starts out with completely normal labs, then progresses to very mild transaminitis. Over time, LFTs can worsen. Rarely it can cause cirrhosis and carcinoma. - Theoretical Tx is just hit the treadmill more and stop eating your dumb fast food.
Alcoholic	<ul style="list-style-type: none"> - Classically AST > ALT. - The ratio need not be 2:1. I've seen variations on NBME forms where there can be very mild transaminitis (i.e., both AST and ALT are <100, with AST only slightly higher than ALT). If the vignette is hyper-easy, they'll say something like AST is 400 and ALT is 200. Both should normally be <50 U/L. - Causes steatosis (fatty liver). - USMLE wants you to know mallory hyaline is seen on biopsy. You don't need to know the image, just this factoid.
Acetaminophen	<ul style="list-style-type: none"> - Acetaminophen overdose most important for USMLE. N-acetylcysteine is antidote. - Breakdown of acetaminophen produces metabolite called NAPQI that depletes reduced glutathione. The latter normally mops up free radicals / prevents oxidation. - Patient will OD on acetaminophen and be asymptomatic for 24-28 hours, then will proceed to get ALT and AST in the tens of thousands + require liver transplant or death. - "N-acetylcysteine regenerates reduced glutathione." Memorize that. - Oxidized glutathione had disulfide bond (-S-S-); reduced glutathione has thiol (-SH). - Activated charcoal should apparently be administered to patients who present very acutely after massive ingestion, as this can ↓ acetaminophen absorption. But I've never

	seen this on NBME. It tends to be more Qbank that's gotcha-style this way. I've only ever seen <i>N</i> -acetylcysteine assessed across NBMEs.
Other drugs	<ul style="list-style-type: none"> - I'd say some important drugs that can cause transaminitis are: - Statins and fibrates, methotrexate, lithium, valproic acid, propylthiouracil. - Mild transaminitis is normal and expected with these agents; the answer is you do not need to decrease dose. - For statins, myopathy is more common than toxic hepatitis (on NBME).

Obgyn-related hepatic issues	
HELLP syndrome	<ul style="list-style-type: none"> - HELLP syndrome = Hemolysis, Elevated Liver enzymes, Low Platelet count. - Can occur as part of severe preeclampsia (HTN + proteinuria after 20 weeks of pregnancy). - Vignette will be pregnant woman >20 weeks of pregnancy where you see the platelets and Hb are low and LFTs are up. Not complicated. - Highest yield point for USMLE is you get schistocytes on a blood smear. USMLE is obsessed with this. - Causes of schistocytes on USMLE = HELLP syndrome, HUS, TTP, DIC, and mechanical heart valves. If you're about to trip out, don't worry, I talk about these conditions in the HY Heme PDF.
Intrahepatic cholestasis of pregnancy	<ul style="list-style-type: none"> - Answer on USMLE for woman in 3rd trimester who gets itchy palms and soles and ↑ serum bile acids. - Cause of 3rd trimester miscarriage. - Treat with ursodeoxycholic acid (ursodiol).
Fitz-Hugh-Curtis Syndrome	<ul style="list-style-type: none"> - Pelvic inflammatory disease (chlamydia or gonorrhea) that has extended to the liver capsule. - USMLE wants you to know this causes fibrin deposition on the liver due to the inflammatory process. This is similar to post-surgical adhesions, where inflammation leads to fibrin deposition.

Heavy metal liver diseases	
Hereditary hemochromatosis	<ul style="list-style-type: none"> - Autosomal recessive; <i>HFE</i> gene; chromosome 6. - Iron overload. - Mechanism USMLE wants is "increased intestinal iron absorption." - Main iron regulation is via shutting off intestinal absorption; this is impaired in hemochromatosis. - Body has poor ability to excrete iron; otherwise there are minor losses via skin shedding. Since women excrete naturally via menses, presentation occurs earlier in men (who clearly don't have this mechanism of excretion). - Can present as "bronze diabetes" → hyperpigmentation due to hemosiderin deposition in skin + ↑ fasting sugars (iron deposition in tail of pancreas). - Miscellaneous other findings can be seen like infertility (iron deposition in hypothalamus, anterior pituitary, or gonads), cardiomyopathy, or arthritis (pseudogout). - Hereditary hemochromatosis, primary hyperparathyroidism, and hypothyroidism are 3 most important causes of pseudogout. I used to only discuss the former two with students over the years, but the latter shows up on a new 2CK NBME exam where they mention chondrocalcinosis (calcium deposition in cartilage). - USMLE wants you to know there is ↑ risk of hepatocellular carcinoma. There is easy NBME Q of hemochromatosis where they ask what patient is at increased risk for, and the answer is simply "hepatocellular carcinoma." - Diagnose with ferritin >300 mg/dL. Transferrin saturation will also clearly be ↑.

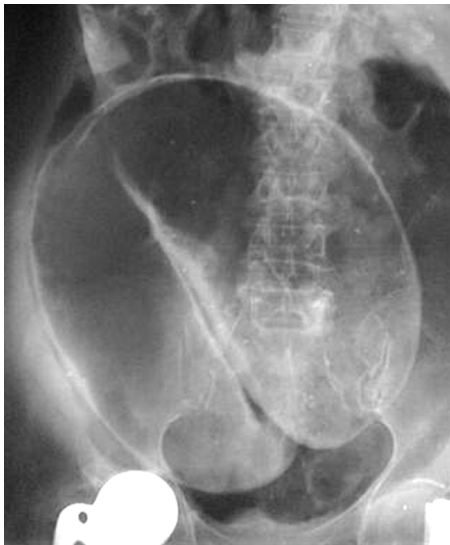
	<ul style="list-style-type: none"> - It is exceedingly rare that ferritin is >300 in other conditions, however this can occur in lymphoma and leukemia, where ↑ ferritin is a poor prognostic marker in non-Hodgkin lymphoma. There is one NBME Q on 2CK where ferritin is 300 where it's not hemochromatosis, but USMLE won't play gotchya. - Treat with serial phlebotomy, not chelators. - Chelators such as deferoxamine or deferasirox are for secondary hemochromatosis due to transfusional siderosis (i.e., repeated blood transfusions that contain iron, for e.g., β-thalassemia major).
Wilson disease	<ul style="list-style-type: none"> - Autosomal recessive. - Copper overload. - Inability to secrete copper into bile from the liver. Copper is normally excreted by the body via secretion into bile. - ↑ urinary copper + ↓ serum ceruloplasmin (copper-binding protein in the blood; in the case of copper overload, body tries to minimize amount carried in blood). - Buzzy / pass-level detail is Keiser-Fleischer rings, which is copper deposited in the cornea of the eye. Vignette can give you what sounds like Wilson disease, and then the answer is "slit-lamp exam." - Can cause ↑ LFTs with cirrhosis and Parkinsonism. - Copper deposits in basal ganglia, especially the putamen. - Parkinsonism in a young patient = Wilson until proven otherwise. - In old patient, Parkinsonism = Parkinson disease, normal pressure hydrocephalus, Lewy-body dementia, or progressive supranuclear palsy. - Treat with the copper chelator penicillamine.

Bowel ischemia	
Ischemic colitis	<ul style="list-style-type: none"> - Patient with cardiovascular disease (CVD) + blood in the stool. - Caused by bleeding at ischemic ulcers at watershed areas in the colon (i.e., splenic flexure and rectosigmoid junction). - Can occur randomly or due to inciting event like recent AAA surgery. - Diagnose with colonoscopy to visualize the ischemic ulcers.
Chronic mesenteric ischemia	<ul style="list-style-type: none"> - Patient with CVD + abdominal pain 1-2 hours after eating meals. - Caused by atherosclerosis of the SMA or IMA → consuming food ↑ oxygen demand of bowel → angina of bowel. - The timing of the pain in relation to meals sounds like duodenal ulcers, however instead of the vignette being a 29-year-old dude from Indonesia with <i>H. pylori</i>, it will be a 69-year-old dude with Hx of coronary artery bypass grafting, intermittent claudication, HTN, and diabetes. - Next best step is "mesenteric angiography" on USMLE.
Acute mesenteric ischemia	<ul style="list-style-type: none"> - Presents 3 different ways on USMLE: 1) Severe abdo pain in patient with AF → LA mural thrombus launches off to SMA or IMA. 2) Severe abdo pain in patient just cardioverted/defibrillated → can launch LA thrombus off to SMA or IMA. There's a Q on 2CK form where this is the case, where they don't mention AF in the stem. 3) Severe abdo pain in patient with Hx of chronic mesenteric ischemia (i.e., acute on chronic) → atheroma within SMA or IMA ruptures, effectively causing an "MI of the bowel." - USMLE wants "mesenteric angiography" as next best step. - Laparotomy is also answer on NBME form. - I've never seen medications or endarterectomy as answers.

GI thromboses	
Mesenteric vein thrombosis	<ul style="list-style-type: none"> - The splenic vein and superior mesenteric vein (SMV) merge to form the portal. The inferior mesenteric vein (IMV) goes to the SMV. - Cirrhosis → ↑ portal venous pressure → ↑ SMV + IMA pressure → stasis. - In addition, any malignancy a patient might have → hypercoagulable state. - NBME Q gives patient with cirrhosis and lung cancer who has abdominal pain + dark, mottled small bowel on surgical examination → answer = “mesenteric venous thrombosis.” Students ask why. I say, “Well there’s ↑ mesenteric venous pressure from the cirrhosis + hypercoagulable state from the malignancy.”
Splenic vein thrombosis	<ul style="list-style-type: none"> - Risk factors are same as above. - As I discussed earlier, USMLE wants you to know splenic vein thrombosis is a cause of esophageal varices due to collateral development with the left gastric vein (which drains the esophageal veins, so if ↑ left gastric venous pressure, then ↑ esophageal venous pressure). - USMLE wants you to know the short gastric veins feed into the splenic vein. So if we have ↑ splenic venous or portal venous pressure, then the short gastric veins also have ↑ pressure.
Budd-Chiari syndrome	<ul style="list-style-type: none"> - Hepatic vein thrombosis. The hepatic vein drains the liver. - Caused by polycythemia vera and pregnancy. - Triad = abdominal pain, ascites, and hepatomegaly.
Portal vein thrombosis	<ul style="list-style-type: none"> - Caused by portal venous stasis from cirrhosis (portal vein enters the liver).

Appendicitis
<ul style="list-style-type: none"> - Triad of RLQ pain, fever, and vomiting (Murphy’s triad). - Pain starts at epigastrium (visceral pain) and migrates toward RLQ (parietal pain). USMLE will ask why there is movement of the pain → answer = “inflammation of the parietal peritoneum.” - Pain at McBurney’s point (1/3 of the way from the anterior superior iliac spine to the umbilicus). - (+) Rovsing sign (pain felt in RLQ upon palpation of LLQ). - USMLE wants you to know appendicitis pain can be RUQ in pregnancy due to displacement of bowel and a shift in appendiceal location. What they will do is tell you pregnant woman in 3rd trimester has RUQ pain, fever, and vomiting + negative abdo ultrasound (meaning not cholecystitis) → answer = “appendicitis.” - “Inflammatory mass and fecalith in the cecum” is phrase used on 2CK NBME form to describe appendicitis. - Diagnosis is done via ultrasound first, and sometimes CT. However, I have not seen USMLE assess either of these, likely because their utility is debated. What I have seen is laparoscopic removal in the stable patient. - USMLE will give ethics/consent Q, where they say patient has operation performed for ovarian procedure but it is seen that she has an acutely inflamed appendix → answer = “remove due to necessity of medical emergency.” - However, if the scenario is reversed and, while performing an appendectomy, the surgeon notices a suspicious lesion on, e.g., one of the ovaries, the answer is “do not biopsy.” Consent must first be obtained for all non-emergencies.

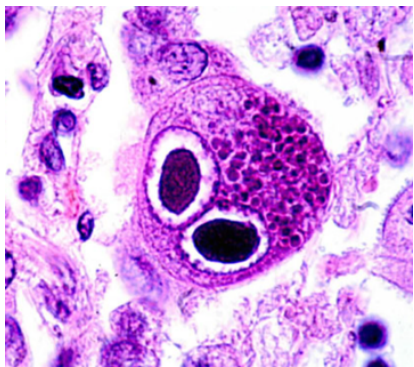
HY colorectal / proctocolonic diagnoses	
Angiodysplasia	<ul style="list-style-type: none"> - Tortuous, superficial vessels in the colonic wall that cause painless bleeding per rectum in elderly. - Classically associated with aortic stenosis (Heyde syndrome; possibly related to pressure backup to the colon). - NBME Q gives older guy arguing with his wife + gets chest pain and bleeding per rectum. Even though colonoscopy is used for diagnosis, they say in this Q that colonoscopy is negative, likely to tell you it’s not cancer causing the bleeding.
Diverticulosis	<ul style="list-style-type: none"> - Mere presence of diverticula in the colon; >50% of people over age 60 in the US.

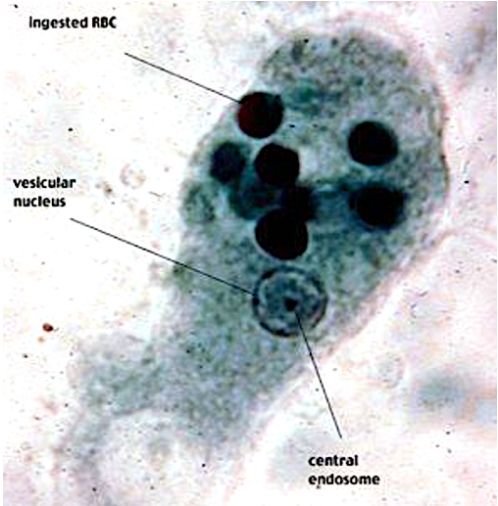
	<ul style="list-style-type: none"> - ↑ straining throughout life leads to herniation of mucosa + submucosa through the muscularis propria of the colonic wall. - Usually asymptomatic, but can bleed. Diverticular bleed is most common cause of painless bleeding per rectum in elderly, followed by colorectal cancer, followed by angiodysplasia. - Can cause colovesical fistula (on new 2CK NBME), where a passageway between the colon and bladder forms, leading to UTI and mixed flora in the urine. - Do not confuse with diverticulitis, which is when a diverticulum becomes inflamed.
Diverticulitis	<ul style="list-style-type: none"> - LLQ pain + fever in patient over 60. One of the highest yield diagnoses on USMLE. - Inflamed diverticulum, usually in the sigmoid colon. - CT of the abdomen with contrast is how to diagnose. - Do not scope acutely, as this can cause perforation. - After patient is treated with antibiotics, a colonoscopy should be scheduled weeks to months later to rule out malignancy. But once again, never scope acutely. - Perforated diverticulitis can require colectomy.
Sigmoid volvulus	<ul style="list-style-type: none"> - Patient over 75 + 2-3 days of constipation + abdo pain. - Rotation around its mesentery causes “dilation of sigmoid colon” (answer on NBME as what is most likely to be seen in patient). - Abdominal x-ray is used to diagnose, which shows a coffee bean sign, which is one of the highest yield radiographic images on USMLE.  <p>The image is an abdominal radiograph (KUB) showing a large, dilated, and twisted loop of the sigmoid colon. This loop has a characteristic 'coffee bean' shape, which is a classic radiographic sign of sigmoid volvulus. The rest of the bowel is relatively collapsed.</p> <ul style="list-style-type: none"> - Tx on NBME is “sigmoidoscopy-guided insertion of rectal tube.”
Fecal impaction	<ul style="list-style-type: none"> - Patient over 70 + chronic constipation + “hard stool palpated in the rectal vault.” - Can sometimes cause fecal incontinence and paradoxical overflow diarrhea leading to encopresis (i.e., word for shitting yo pants). - Idiopathic, but exacerbated by opioids. - Treatment is with enema and laxatives.
Hemorrhoids	<ul style="list-style-type: none"> - Bleeding per rectum that will be described as “blood on the toilet paper,” or “blood that drips into the toilet bowl.” - Hemorrhoids are technically normal vascular structures within the anal canal that facilitate/cushion the passage of stool. - Bleeding from internal hemorrhoids is painless. These are above the pectinate line in the anal canal. - Bleeding from external hemorrhoids is painful. These are below the pectinate line. - Pregnancy and cirrhosis are risk factors. - 2CK NBME wants rectal exam followed by anoscopy for diagnosis.

	<ul style="list-style-type: none"> - Hemorrhoids often self-resolve and can be managed conservatively with sitz bath, NSAIDs, and ↑ dietary fiber. However, if USMLE forces you to choose surgical management for more severe cases, the answer is rubber band ligation.
Anal fissure	<ul style="list-style-type: none"> - Young adult who has painful bowel movements +/- blood in the stool. - The key detail is they refuse the rectal exam because the pain is so bad. - For whatever reason, they can also say there's an associated skin tag. I've seen this more than once, where the student says, "What's with the skin tag?" No fucking idea. - Mechanism can be "increased anal sphincter tone." - Tx on 2CK Surg is sitz bath. - If the USMLE forces you to choose a med, topical nitrates or diltiazem is used.
Pilonidal cyst/abscess	<ul style="list-style-type: none"> - Answer on USMLE for cystic mass at the superior aspect of the gluteal cleft. - Contains hair; often caused by ingrown hairs. - Tx on 2CK Surg = incision and drainage.
Perianal abscess	<ul style="list-style-type: none"> - Answer on USMLE for painful, erythematous mass near anal verge. - Increased risk in Crohn and diabetes. - Tx on 2CK Surg = incision and drainage.
Anal malignancy	<ul style="list-style-type: none"> - 2CK Surg Q gives cancer at anal verge + asks for next best step in management → answer = colonoscopy; excision is wrong answer. Presumably the scoping is done to first investigate the extent of the disease, as that might alter management.


HY GI bacterial infections	
Gram-negative rods	
ETEC	<ul style="list-style-type: none"> - Enterotoxigenic <i>E. coli</i> causes traveler's diarrhea. - Will present as brown/green diarrhea in person who's gone to Mexico or Middle East classically.
EHEC	<ul style="list-style-type: none"> - Enterohemorrhagic <i>E. coli</i> causes bloody diarrhea 1-3 days after consumption of beef. - Produces shiga-like toxin, which can cause hemolytic uremic syndrome (HUS; triad of renal dysfunction, schistocytosis, and thrombocytopenia).
<i>Shigella</i>	<ul style="list-style-type: none"> - Bloody diarrhea 1-3 days after consumption of beef. - Also can cause HUS via shiga toxin.
<i>Salmonella</i>	<ul style="list-style-type: none"> - Food poisoning is caused by <i>Salmonella typhimurium</i> and <i>Salmonella enteritidis</i>. The nomenclature has changed with time, but those names are acceptable. - Bloody diarrhea 1-3 days after infection from consuming poultry, or following exposure to eggs or reptiles (i.e., turtles, lizards, etc.). New NBME Q mentions bloody diarrhea in someone with a pet lizard. - <i>Salmonella typhi</i> causes typhoid fever, which will be rose spots on the abdomen in a patient who's "prostrated" (i.e., lying down in pain); can be either diarrhea or constipation. The reservoir for <i>S. typhi</i> is humans, not chickens/reptiles.
<i>Vibrio</i>	<ul style="list-style-type: none"> - <i>Vibrio cholerae</i> (cholera) presents as "liters and liters" of rice-water stool in someone who went traveling to, e.g., Mexico. The way you can differentiate this from ETEC traveler's diarrhea is that cholera is notably profusely high-volume. - Acquired fecal-oral (i.e., fecal-contaminated food/water). - Both ETEC and cholera vignettes can tell you the patient has 8-12 stools daily, so it's not the # of stools that matters; it's the emphasis on volume. Cholera causes death via severe dehydration and electrolyte disturbance. - Tx is oral rehydration on USMLE; if patient has low BP or altered mental status (i.e., confusion/coma), IV hydration is done. - <i>Vibrio parahaemolyticus</i> doesn't cause profuse, watery diarrhea the same way cholera does. I've seen this organism asked once in an NBME vignette where the patient ate sushi (can be acquired from sushi and shellfish).

	<ul style="list-style-type: none"> - <i>Vibrio vulnificus</i> causes severe sepsis in half of patients. This is asked on offline NBME 19 where a dude went running on a beach and got sepsis, with no mention of consumption of food. But it's apparently acquired from shellfish.
<i>Yersinia enterocolitica</i>	<ul style="list-style-type: none"> - Causes bloody diarrhea + either appendicitis-like (i.e., RLQ) pain or arthritis. - The RLQ pain is from mesenteric adenitis or terminal ileitis. - Toxin has same MOA as ETEC heat-stable toxin (i.e., ↑ cGMP).
<i>Campylobacter jejuni</i>	<ul style="list-style-type: none"> - Bloody diarrhea 1-3 days after consumption of poultry. - Can cause Guillain-Barre syndrome (ascending paralysis + ↓ tendon reflexes + albuminocytologic dissociation in the CSF → Tx with IVIG + plasmapheresis). - Grows best at high temperatures (42 degrees).
Gram-positive rods	
<i>Bacillus cereus</i>	<ul style="list-style-type: none"> - Watery diarrhea and/or vomiting in patient who's consumed reheated or fried rice. The process of heating/re-heating causes germination of spores. - Can also cause eye infections (weird, but on USMLE). They'll say patient who's had eye surgery + now has infection caused by gram(+) rod → will be only gram(+) rod listed.
<i>Clostridium perfringens</i>	<ul style="list-style-type: none"> - Watery/secretory diarrhea following consumption of poultry. - Causes gas gangrene (CO₂ gas) due to production of α-toxin/phospholipase; presents as black skin / crepitus. - Can also cause emphysematous cholecystitis (air in gall bladder wall).
<i>Clostridium difficile</i>	<ul style="list-style-type: none"> - Diarrhea (pseudomembranous colitis) ~7-10 days after commencing oral antibiotics. - Antibiotics kill off normal bowel flora, allowing <i>C. difficile</i> to overgrow. - <i>C. difficile</i> is not normal flora, however. It is acquired via consumption of spores. - Can be watery or bloody diarrhea on NBME. Can also cause LLQ cramping (not RLQ as with <i>Yersinia</i>). - There is NBME Q where they say 28-year-old with LLQ cramping and bloody diarrhea 7 days after starting oral antibiotics → answer = <i>C. diff</i>; wrong answer is <i>Yersinia</i>. - USMLE doesn't care which antibiotics cause it; can be any. - Diagnose with stool AB toxin test; stool culture is wrong answer. - Treat with oral vancomycin. - Vancomycin has poor oral bioavailability, so is usually given IV for things like endocarditis and meningitis. But for <i>C. diff</i> infection, <i>that's a good thing</i> because we want it to stay within the GI tract. - Other fancy Abx like fidaxomicin, rifaximin, etc., I've never seen on NBME. More just masturbation around dumb factoids.
Gram-positive cocci	
<i>Staph aureus</i>	<ul style="list-style-type: none"> - <i>S. aureus</i> pre-formed heat-stable toxin is acquired from two main sources on NBME: 1) various meats sitting under a heat lamp / out for long periods of time, e.g., at a buffet; 2) dairy products like creams, custards, potato salad. - Notably causes vomiting 1-6 hours after consumption. This is notable, as the symptoms occur rather quickly. Diarrhea, both watery and bloody, can occur, but is not mandatory. The main crux is the vomiting.
Other GI bacteria	
<i>Tropheryma whipplei</i>	<ul style="list-style-type: none"> - Causes Whipple disease, a GI malabsorptive syndrome where the patient can also get arthritis and renal and cardiac disease. - 100% of Qs will say "PAS-positive macrophages in the lamina propria." - New highly pedantic Q on 2CK NBME 10 wants "ceftriaxone + daily TMP/SMX for one year" as the treatment. Organism isn't even HY. No idea why they care.
Tropical sprue	<ul style="list-style-type: none"> - Causes flattening of villi similar to Celiac, but considered infective/bacterial in origin. Literature says exact etiology not certain. - Answer on USMLE for patient living in tropical area with unknown malabsorptive disease, where you can easily eliminate the other answers. - Tx = tetracycline.

HY GI viral infections	
Rotavirus	<ul style="list-style-type: none"> - Most common cause of watery diarrhea in unvaccinated children < 5 years. - Vaccine normally given orally at 2, 4, and 6 months of age.
Norwalk virus	<ul style="list-style-type: none"> - Most common cause of watery diarrhea in adults and rotavirus-vaccinated children. - Cruise ships and business conferences are buzzy places to acquire (fecal-oral); basically any place with high density of people. - If the Q says a young child + family all have watery diarrhea, the answer is Norwalk, not Rota, since only the young child would get Rota, not the family also.
Herpes	<ul style="list-style-type: none"> - HSV1/2 causes herpes esophagitis → odynophagia + punched-out ulcers in esophagus.
CMV	<ul style="list-style-type: none"> - CMV esophagitis → odynophagia + linear (confluent) ulcers in esophagus. - CMV colitis → bleeding per rectum in AIDS patient with CD4 count <50. - CMV retinitis → blurry vision in HIV (or immunosuppressed) patient. - Most common organism transmitted via blood transfusions and organ transplants. - USMLE likes “intranuclear inclusions” or “intranuclear inclusion bodies” for CMV. This refers to the “owl eyes” that can be seen on histo. 

HY GI protozoal infections	
<ul style="list-style-type: none"> - A protozoan is a unicellular eukaryote. - ECG → <i>Entamoeba histolytica</i>, <i>Cryptosporidium parvum</i>, and <i>Giardia lamblia</i> are all GI protozoa that are acquired via cysts in water (i.e., they are water-borne). If “water-borne” and “fecal-oral” are both listed as answers, USMLE wants “water-borne” as means of acquisition. 	
<i>Entamoeba histolytica</i>	<ul style="list-style-type: none"> - Bloody diarrhea in person who went to Mexico. - Can cause “flask-shaped ulcers” in the small bowel and liver abscess. - Demonstrates “erythrophagocytosis,” where RBCs can be seen within it on LM. 

	<ul style="list-style-type: none"> - Treat with metronidazole. - Iodoquinol kills intraluminal parasite.
<i>Cryptosporidium parvum</i>	<ul style="list-style-type: none"> - Watery diarrhea in person who went to Mexico. - Appears as acid-fast cysts (same stain as TB).  <ul style="list-style-type: none"> - Self-limiting in immunocompetent persons → Tx = supportive care. - Chronic diarrhea in HIV → Tx = nitazoxanide.
<i>Giardia lamblia</i>	<ul style="list-style-type: none"> - Steatorrhea in person who went to Mexico. - Steatorrhea = bloating + extremely foul-smelling stool that floats. - The steatorrhea is due to <i>Giardia</i> causing malabsorptive diarrhea. - There is one NBME Q for <i>Giardia</i> where they say “foul-smelling watery diarrhea with bloating,” which is audacious, since 9 times out of 10 it is not described as watery. But the “bloating” and “foul-smelling” are consistent with steatorrhea in this context. Just letting you know it exists. - Acquired via fresh water lakes / scuba diving. There is a <i>Giardia</i> NBME Q where they say a woman goes scuba diving in Mexico and then gets foul-smelling stools with bloating. Student says, “Wait but I thought <i>Giardia</i> was fresh water. If she went scuba diving in the ocean then how is that <i>Giardia</i>?” → People can go scuba diving in fresh water lakes too bro. Don’t know what to tell you. - Flagellated protozoan. USMLE wants you to know the images for both the cyst as well as the flagellated trophozoite.  <p>Cyst form of <i>Giardia</i>. Not dramatic.</p>

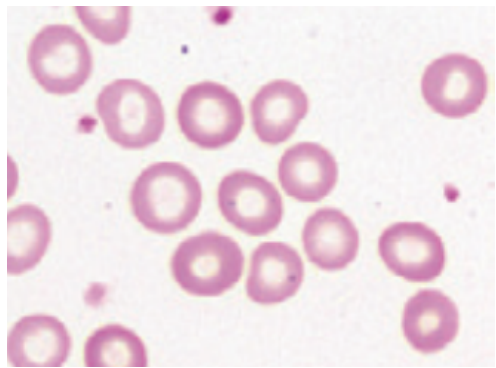
	 <p>Trophozoite form of <i>Giardia</i>.</p> <p>- Tx = metronidazole.</p>
--	--

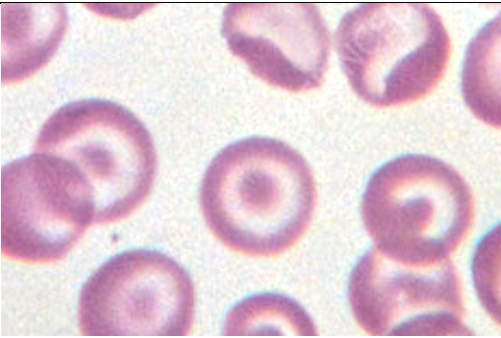
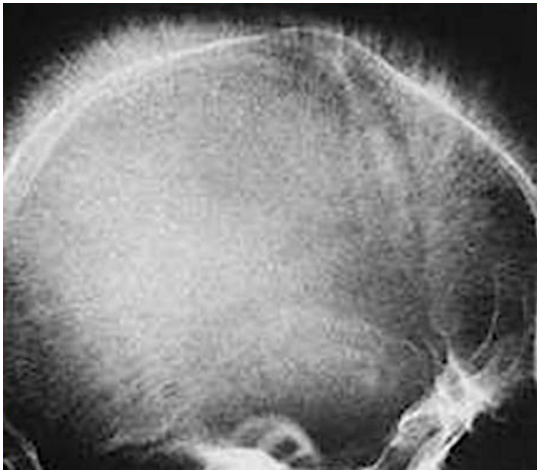
HY GI parasitic (helminth) infections	
<ul style="list-style-type: none"> - USMLE wants you to know routes of acquisition for the nematodes (i.e., ingested or through feet, etc.). - You do not need to obsess over exactly which anti-helminthic agent treats which organism. Waste of time. What USMLE wants you to know is the big-picture concept that -bendazoles (i.e., mebendazole) and pyrantel pamoate are the two agents that treat nematodes primarily. -Bendazoles microtubules (tubulin) and pyrantel pamoate causes helminth paralysis. - Praziquantel is used for cestodes and trematodes. It causes helminth paralysis. - Albendazole is the odd one out that is used for neurocysticercosis (<i>Taenia solium</i>; cestode). - USMLE doesn't give a fuck about diethylcarbamazine. 	
Nematodes (roundworms)	
<i>Ascaris lumbricoides</i>	- Ingested . Giant roundworm; causes intestinal obstruction. (Ascariasis)
<i>Enterobius vermicularis</i>	- Ingested . Causes perianal itching / (+) tape test in children. (Enterobiasis)
<i>Angiostrongylus</i>	- Ingested by eating raw slugs/snails. Causes eosinophilic meningitis.
<i>Trichinella spiralis</i>	- Ingested by eating pork/ bear meat. Causes triad of fever, periorbital edema, and myalgias. (Trichinosis)
<i>Strongyloides stercoralis</i>	- Acquired through soil/one's feet . Causes intestinal obstruction + pulmonary symptoms (apparently travels to lungs via blood, then travels up respiratory tree into esophagus, where it is swallowed).
Hookworms	<ul style="list-style-type: none"> - Acquired through soil/one's feet. "Hookworms" refers to <i>Ancylostoma duodenale</i> and <i>Necator americanus</i>. - Cause microcytic anemia / ↓ hemoglobin due to sucking blood in GI tract.
Cestodes (tapeworms)	
<i>Diphyllobothrium latum</i>	- Fish tapeworm. Nothing else you need to know.
<i>Taenia solium</i>	- Pork tapeworm. Causes cysticercosis (muscle pain/cysts) + neurocysticercosis ("Swiss cheese" appearance of brain or soap bubbles in ventricles).
<i>Echinococcus granulosus</i>	<ul style="list-style-type: none"> - Aka hydatid worm, or dog tapeworm; causes hydatid cyst disease. - Acquired from dogs (clearly). - Causes liver cysts. Only point you need to know is that you do not biopsy because this can cause anaphylaxis. Tx = surgically remove.
Trematodes (flukes)	
<i>Schistosoma</i>	<ul style="list-style-type: none"> - Penetrates skin when swimming; snail is host. - <i>Schistosoma mansoni/japonicum</i> can cause portal hypertension. Not HY but shows up once on NBME. Not to be confused with <i>Schistoma hematobium</i>, which causes squamous cell carcinoma of the bladder.
<i>Paragonimus westermani</i>	<ul style="list-style-type: none"> - Ingested from crab meat or crayfish. - Aka lung fluke. Most common cause of hemoptysis in the world.
<i>Clonorchis sinensis</i>	- Ingested from fish. Causes cholangiocarcinoma.

GI pharm basics for IM	
PPIs	<ul style="list-style-type: none"> - Omeprazole. - Shut of proton pumps on parietal cells → ↓ acid secretion. - Irreversible and non-competitive; more efficacious than H2 blockers, which are reversible and competitive. - Choose PPIs over H2 blockers for Tx of most things, like GERD, ulcers, and <i>H. pylori</i>. - Diagnosis of GERD is 2-week trial of PPIs. - PPIs cannot be given with sucralfate or -azole antifungals (on NBME).
H2-blockers	<ul style="list-style-type: none"> - Cimetidine, ranitidine. - Not used often. PPIs more efficacious. - One 2CK form has “2-week trial of H2 blocker” as correct for diagnosis of GERD, but PPIs aren’t listed. As I said above though, if you’re forced to choose between a PPI and H2 blocker, the PPI is correct basically always. - Cimetidine can cause gynecomastia and inhibits P-450.
Metoclopramide	<ul style="list-style-type: none"> - As discussed earlier, anti-emetic + prokinetic agent (means ↑ peristalsis). - D2 antagonist but also an antagonist of serotonin 5HT3 and agonist of 5HT4 receptors. The effects on serotonin receptors ↑ gut peristalsis. - HY use on USMLE is diabetic gastroparesis (i.e., sounds like GERD but patient has severe diabetes, where answer is metoclopramide, not PPI).
Ondansetron	- Powerful anti-emetic classically used for nausea/vomiting from chemoradiotherapy.
Erythromycin	- Motilin receptor agonist that can be used for diabetic gastroparesis, unrelated to its antibiotic utility as a macrolide.
Misoprostol	<ul style="list-style-type: none"> - PGE1 analogue. Used for NSAID-induced ulcers after PPIs. - NSAIDs ↓ prostaglandins. Therefore misoprostol is the replenished prostaglandin. - Prostaglandins ↓ acid production, ↑ mucous and bicarb production, and ↑ gastric mucosal blood flow.
Magnesium	- Antacid. Causes diarrhea.
Aluminum.	- Antacid. Causes constipation (“Aluminum amount of feces.”)
Calcium	<ul style="list-style-type: none"> - Antacid. Causes milk-alkali syndrome (↑ Ca^{2+} + ↑ HCO_3^- + urolithiasis). - Bisphosphonates (e.g., alendronate) and tetracyclines (e.g., doxycycline) cannot be taken with calcium or iron supplements (i.e., divalent cations), since the latter chelate the drugs and ↓ absorption / oral bioavailability. USMLE loves this. - USMLE will give you, e.g., prostatitis treated with ciprofloxacin, + list all sorts of other meds the patient is on, as well as a calcium supplement, and then tell you the patient’s condition isn’t improving + ask why → answer = calcium carbonate.
Bismuth	- Can be used as part of <i>H. pylori</i> regimens (but not first-line).
Sucralfate	<ul style="list-style-type: none"> - Can be used to coat ulcers / form a barrier to protect against acid and ↓ pain. - Cannot take with PPIs. The latter ↓ ability of sucralfate to crosslink/work correctly.
5-ASA compounds	- Mesalamine, sulfasalazine; NSAIDs used for IBD, as discussed earlier.
TNF- α blockers	<ul style="list-style-type: none"> - Infliximab, adalimumab, and etanercept. - USMLE likes these for IBD <i>after</i> 5-ASA compounds and steroids are attempted. - Infliximab and adalimumab are monoclonal antibodies against TNF-α. - Etanercept is a recombinant receptor that mops up soluble TNF-α.
Octreotide	<ul style="list-style-type: none"> - Somatostatin analogue used for esophageal varices Tx after banding. - Acts by ↓ portal blood flow.
Propranolol	- Beta-blocker that can be used for esophageal varices prophylaxis (not Tx).
Lactulose	<ul style="list-style-type: none"> - Used to Tx hyperammonemia in cirrhosis. - Carbohydrate that is metabolized by gut bacteria into acidic substrates that trap ammonia as ammonium. The latter is then excreted (ions aren’t absorbed as easily). - The answer on USMLE is “acidification, NH_4^{++}” for what lactulose causes in the gut.
Neomycin	<ul style="list-style-type: none"> - Used to Tx hyperammonemia in cirrhosis. - Antibiotic that kills ammonia-producing bacteria.
Loperamide	<ul style="list-style-type: none"> - Mu-opioid receptor agonist used to treat diarrhea-predominant IBS. - Opioids cause constipation, so “this is a good thing” in this case.
Ezetimibe	- Blocks cholesterol absorption in the small bowel.

Cholestyramine	- Bile acid sequestrant. Causes reduced enterohepatic circulation of bile acids at terminal ileum → liver must now convert more cholesterol into bile acids in order to replenish them → liver pulls cholesterol out of the blood to accomplish this.
Orlistat	- Pancreatic lipase inhibitor used for obesity; can cause steatorrhea.
Nystatin	- Mouth wash used for oropharyngeal candidiasis.
Fluconazole	- Used for candidal esophagitis.
Acyclovir	- HSV esophagitis; HSV1/2 causes “punched out” ulcers.
Ganciclovir	- CMV esophagitis and colitis; causes linear/confluent ulcers. Same MOA as acyclovir.
CAP	- Clarithromycin, Amoxicillin, PPI. - First-line Tx for <i>H. pylori</i> . - If patient still has (+) urease breath test after 4 weeks, assume antibiotics resistance and switch out the CA and add tetracycline, metronidazole, and bismuth (keep PPI).
Vancomycin	- Given orally to treat <i>C. difficile</i> .
Metronidazole	- “Anaerobes below the diaphragm.” - Used for diverticulitis in combo with a fluoroquinolone. - Tx for <i>Giardia</i> + <i>Entamoeba</i> .
Imipenem	- Carbapenem antibiotic that has fantastic penetration for pancreatitis.
Mebendazole	- Used for most nematodes (i.e., <i>Ascariasis</i> , <i>Enterobiasis</i> , hookworms, etc.).
Albendazole	- Same as mebendazole, but for whatever reason it’s known as a preferred agent for neurocysticercosis, which is caused by a cestode (<i>Taenia solium</i>).
Pyrantel pamoate	- Agent used against nematodes. Shows up on an offline NBME as answer.
Praziquantel	- Used for cestodes and trematodes.

IM Heme/Onc

Iron deficiency anemia vs thalassemia			
Variable	IDA	Thalassemia	HY points
Hb	↓	↓	- Thalassemia means abnormal synthesis of either the α or β globin chain. It presents two ways on USMLE: 1) As a microcytic anemia despite normal iron + ferritin; or 2) As a patient who has a microcytic anemia despite iron supplementation. - Most IDA is seen in menstruating women, even if their menses aren't heavy. 2CK will actually explicitly say menses are normal/not heavy, but Dx is still IDA. - NBME will give you microcytic anemia in a woman who's 32, and then the answer is just "check serum iron and ferritin." This is because thalassemia is often misdiagnosed as IDA, where if we get the iron studies back and see iron + ferritin are normal, we say, "Ok that's thalassemia, not IDA." → next best step = hemoglobin electrophoresis. - 2CK forms like to give pregnant women at first antenatal screening with microcytic anemia who are given iron for 3 weeks but show no improvement. Q won't mention anything about patient's iron or ferritin levels. So you say, "Ok, this is a microcytic anemia despite iron supplementation, meaning the iron + ferritin are actually normal, so this is thalassemia." → next best step = hemoglobin electrophoresis.
MCV	↓	↓	
Serum iron	↓	Normal	
Ferritin	↓	Normal	
Hb electrophoresis	Normal	α : normal; β : ↑ HbA2 + HbF (See discussion at bottom of table)	
What happens if we give iron?	Improvement	No improvement (HY)	
RDW	↑ (HY)	↓/Normal (HY)	- Red cell distribution width. - All you need to know is, basically always, ↑ RDW means IDA straight-up 9/10 Qs. - The only Q where ↑ RDW is seen in thalassemia is on CMS FM form 4, where IDA is wrong, but they give ferritin within the normal range, so IDA isn't possible. But the ↑ RDW is essentially an erratum, as this is rare as fuck. - Therefore we can essentially say that ↑ RDW is sensitive but not specific for IDA, where if RDW isn't ↑, we can rule-out IDA, but be careful about automatically saying "must be IDA" if RDW is ↑.
Blood smear	Pale RBCs	Target cells	- IDA causes pale RBCs (i.e., ↑ central pallor). Not dramatic.  - Target cells are highly buzzy and pass-level for thalassemia. Probably 14/15 Qs on USMLE mentioning target cells are thalassemia (α or β).

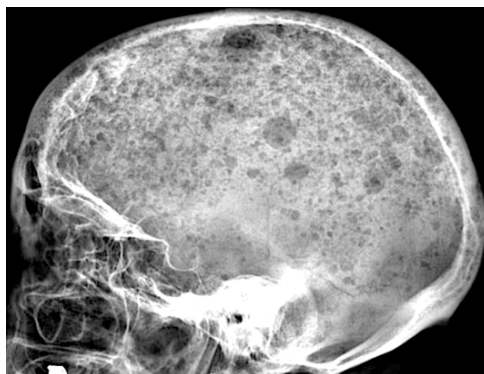
			 <p>- There is one NBME Q with target cells in a splenectomy patient, but they're a background finding and don't facilitate answering the Q in any way.</p>
Tx	Iron	Transfusions if severe	<p>- Oral iron is ideal over parenteral (IV) or intramuscular iron always. I mention this because answers such as "parenteral iron" are wrong/distractors basically always. I'll say to a student, "You want to give this patient IV iron?"</p> <p>- Oral iron can cause constipation and black stools. USMLE wants you to know iron, aluminum (antacid), and verapamil all cause constipation.</p> <p>- Transfusional siderosis (secondary hemochromatosis) is sophisticated way of saying iron overload due to repeated blood transfusions, e.g., in β-thalassemia major. Each RBC transfusion contains iron. Use chelators (e.g., deferoxamine) to treat.</p>
<p>- Thalassemia is impaired synthesis of either the α- or β-globin chain in hemoglobin.</p> <p>- α-thalassemia can have 1-4 alleles mutated; β has 2. Don't worry about obscure intermediate types, etc.</p> <p>- USMLE overwhelmingly focuses on adults for both α- and β-thalassemia, since these patients are usually misdiagnosed as having iron deficiency anemia. That's why you need to know about thalassemia, so you don't misdiagnose patients with IDA.</p> <p>- Adults with α-thalassemia will be asymptomatic (1 mutation), where they have an incidental microcytic anemia picked up on antenatal screening. Adults with 2 mutations have symptoms akin to IDA, but they'll fail to improve with iron supplementation.</p> <p>3 α mutations (HbH disease; β_4 tetramer) will present as a sick kid; 4 α mutations (Hb Barts; γ_4 tetramer) will be fatal <i>in utero</i>.</p> <p>- β-thalassemia minor will be 1 mutation in an adult who presents similar to 2 α-thalassemia mutations (i.e., similar to IDA).</p> <p>- β-thalassemia major is 2 mutations and will present as a sick kid similar to 3 α-thalassemia mutations.</p> <p>- It is exceedingly HY you know that β-thalassemia has \uparrow HbA2 (α_2/δ_2) and HbF (α_2/γ_2); α-thalassemia (1 or 2 mutations) has a normal hemoglobin electrophoresis.</p> <p>- Sick children with thalassemia are known to get "chipmunk facies/skull" and hepatosplenomegaly occur due to $\uparrow\uparrow$ extramedullary hematopoiesis.</p> 			

Anemia of chronic disease (AoCD)

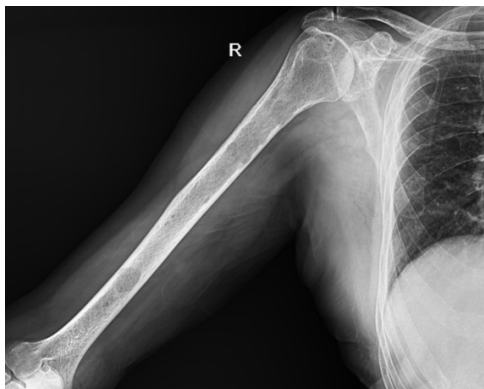
- The answer on USMLE for anemia (\downarrow Hb) in patient who has **renal failure**, an autoimmune disease (i.e., RA, JRA, IBD, SLE, etc.), hepatitis B/C, HIV, or malignancy.
- Patients will have low iron but **normal ferritin** (or sometimes slightly high). Ferritin is the most sensitive marker of iron stores, which means these patients are not iron deficient.
- There's two main reasons iron is low in AoCD: 1) RBC production is decreased because cytokines (namely IL-6 and TNF- α) block iron release from storage sites, and 2) hepcidin, a molecule produced by the liver, decreases gut absorption of iron and promotes its storage in cells instead.
- It's to my observation that **renal failure** is the highest yield cause of AoCD on USMLE. This is due to "cytokine-mediated EPO deficiency." This is an answer on an NBME form. EPO is the treatment for AoCD only if renal failure is the etiology. Otherwise the Tx is merely addressing the underlying condition (e.g., the RA), and EPO is a wrong answer.
- There is an AoCD NBME Q for RA where they ask how to treat and answer is "no specific measures indicated." Student says, "Wait, I thought we were supposed to address the underlying condition, so I was confused by this answer choice." I agree. So don't take it up with me. Take it up with NBME.
- One of the highest yield points I can communicate is that even though classic MCV is normal in AoCD, it will be \downarrow in ~50% of NBME Qs. I've seen students say, "Oh it can't be AoCD cuz MCV is low." No. USMLE loves giving low MCV in AoCD, especially on 2CK forms. I've seen MCVs of 72 and 75 in JRA Qs.

Multiple myeloma

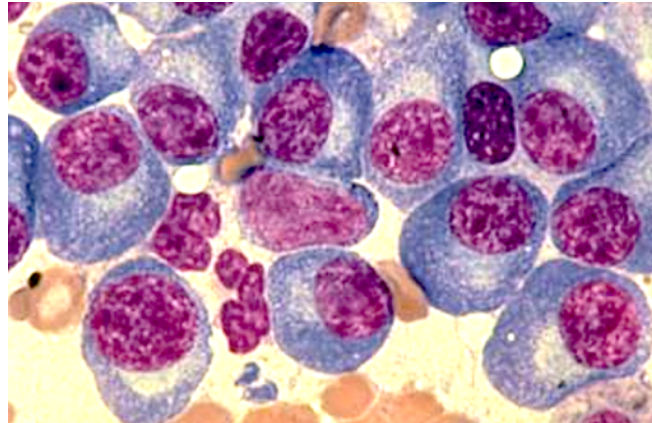
- Cancer of plasma cells.
- Plasma cells normally secrete immunoglobulins, so we have $\uparrow\uparrow$ serum immunoglobulins.
- Multiple myeloma buzzy presentation is patient over 50 with mid-back pain + hypercalcemia.
- \uparrow serum Ca^{2+} occurs due to lytic lesions of bone caused by the proliferating plasma cells. This can present as pathologic rib fractures or "pepper pot skull."



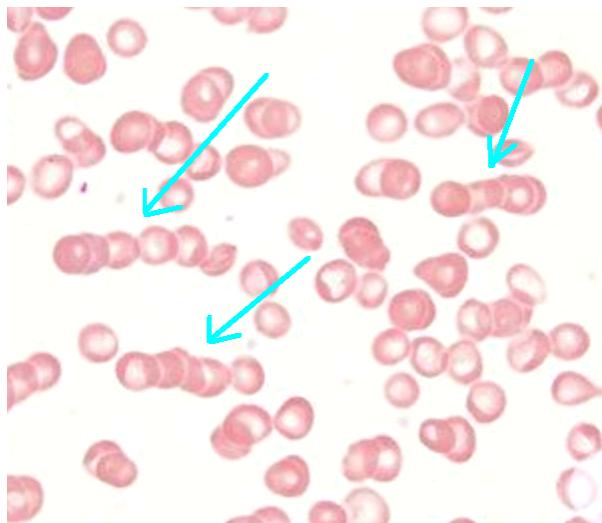
- There is NBME Q floating around where they give lytic lesions of the humerus as well; not buzzy/textbook in comparison to rib/skull lesions, but they show image similar to following:



- First step in diagnosis is **serum protein electrophoresis (SPEP)**, which shows ↑↑ serum IgG kappa or lambda light chains. This is known as an M-spike (monoclonal spike; this does not mean IgM). Then **bone marrow biopsy** confirms the diagnosis, showing >10% plasma cells.
- Smear in multiple myeloma will show plasma cells (blue cells below) with “clockface chromatin,” which is the appearance ascribed to the nuclei (purple below).



- Urinalysis will show Bence Jones proteinuria, which is simply the IgG light chains in the urine.
- Amyloidosis is proteins depositing where they shouldn't be depositing. Immunoglobulins are proteins. Since these are flying around in the blood, they deposit in the heart (**cardiac amyloidosis**; S4 heart sound with diastolic dysfunction) and kidney (**renal amyloidosis**; nephrotic syndrome).
- The IgG light chains stick to RBCs, causing the RBCs to stick to each other as stacks (i.e., Rouleaux). These are heavy and sediment quickly on centrifugation, hence ↑ ESR. USMLE can show you a picture of the Rouleaux rather than the clockface chromatin, where you need to know instantly the diagnosis is MM.



- MCV can sometimes be ↑ in MM (e.g., 108; NR 80-100). Don't be confused by this. It is common. This is caused by 1) ↑ immunoglobulins being transported by RBCs (thereby ↑ RBC size); 2) ↓ RBC production within bone marrow due to infiltrating plasma cells, causing ↑ RBC size to compensate; and 3) B9 and B12 deficiencies can be caused by MM.
- Tx is initially IV bisphosphonate to ↓ risk of bone lysis.
- Should be noted that patients with bone marrow biopsy showing <10% plasma cells have a condition known as MGUS (monoclonal gammopathy of undetermined significance). There is small annual risk of progression to multiple myeloma. These patients might have fatigue and/or ↑ MCV but no hypercalcemia or renal dysfunction.

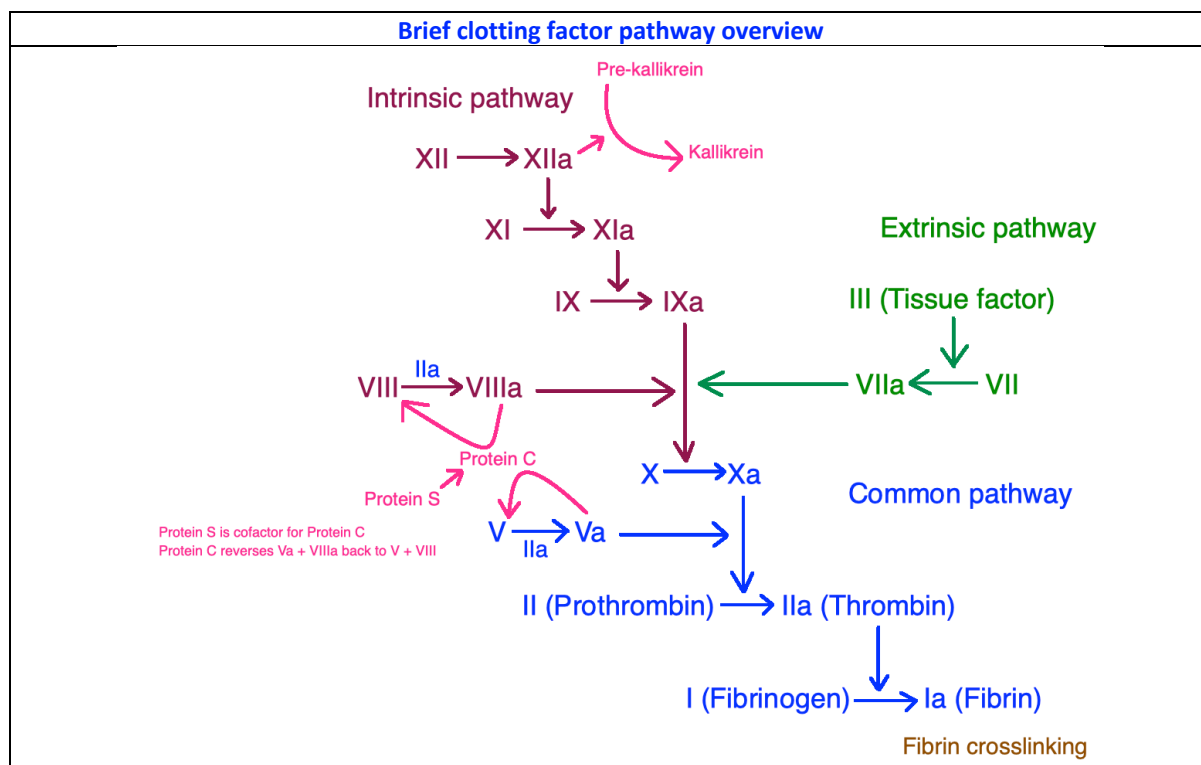
Waldenstrom macroglobulinemia

- Cancer of plasmacytoid cells.
- “-Oid” means looks like but ain’t. So these are cells that look like plasma cells but they ain’t plasma cells.
- Causes IgM M-protein spike on SPEP (MM is IgG M-protein spike).
- In contrast to MM, does not cause hypercalcemia, lytic lesions, Bence-Jones proteinuria, or amyloidosis.
- Waldenstrom causes **hyperviscosity syndrome**, which will present as headache, blurry vision, tinnitus, or Raynaud phenomenon.

Polycythemia vera vs secondary polycythemia

Polycythemia vera	<ul style="list-style-type: none"> - JAK2 mutation causing “proliferation of hematopoietic stem cells” (answer on NBME). - Qs will give \uparrow Hb at 18+ (NR 12-17.5 g/dL) <i>and</i> \uparrow WBCs and/or platelets. - In other words, at least 2/3 cell lines will be \uparrow, with RBCs always \uparrow. - \uparrow Hb can cause hyperviscosity syndrome. - Basophilia can cause pruritis after a shower. - EPO is suppressed due to \uparrow Hb. - USMLE wants phlebotomy as the answer to \downarrow acute symptoms associated with hyperviscosity syndrome (i.e., “What is next best step to \downarrow patient’s headache / blurry vision?”). - Serial phlebotomy and hydroxyurea can be answers to \downarrow recurrent symptoms; the USMLE will not give both at the same time.
Secondary polycythemia	<ul style="list-style-type: none"> - Isolated \uparrow in RBCs due to \uparrow EPO – i.e., WBCs and platelets are normal. - Seen in those with lung disease where arterial O₂ tension is low \rightarrow kidneys sense \downarrow O₂ and secrete EPO \rightarrow acts on bone marrow to stimulate erythroid precursors. - Also seen in renal cell carcinoma, which can secrete EPO (and PTHrp causing hypercalcemia). - Exogenous administration (e.g., cyclists).

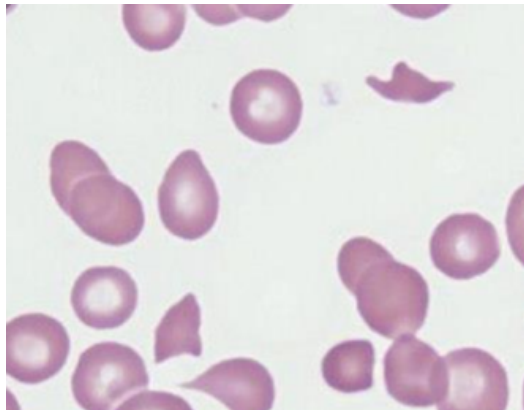
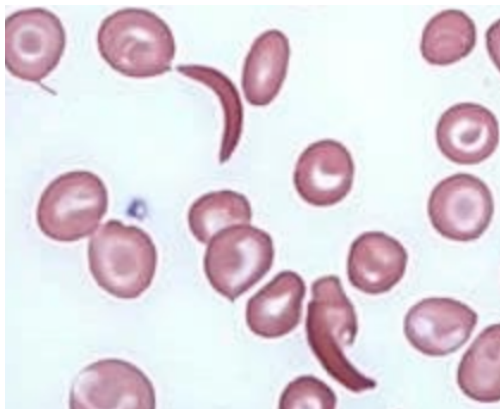
Brief clotting factor pathway overview



- Prothrombin time (PT) reflects the functioning of the extrinsic pathway; activated partial thromboplastin time (PTT; aPTT) reflects intrinsic pathway.
- In other words, if PT alone is high, then the **extrinsic pathway** is fucked up.
- If PTT alone is high, then the **intrinsic pathway** has a problem.
- If both PT and PTT are elevated, then the **common pathway** has an issue.
- **Normal PT is 10-15 seconds.**
- **Normal PTT is 25-40 seconds.**
- **Normal bleeding time is 2-7 minutes.**
- Bleeding time relates to **platelets** and has nothing to do with clotting factors.
- PT and PTT relate to clotting factors and have nothing to do with platelets.

HY Core DDx for IM	
ITP	<ul style="list-style-type: none"> - Idiopathic/immune thrombocytopenic purpura. - Antibodies against glycoproteins IIb/IIIa on platelets. - Causes ↓ low platelets; ↑ bleeding time; no change PT and PTT. - Bleeding time is high because platelets are fucked up. PT and PTT are normal because these refer to clotting factors, which have nothing to do with ITP. - Normal platelet count is 150-450,000/μL. Platelets in ITP Qs are usually <100,000. - Precipitated by viral infection, where antibodies against viral proteins cross-react with platelets (disrupts platelet aggregation); type II hypersensitivity. - Viral infection will be asymptomatic in ~50% of vignettes. In other words, the Q need not mention the viral infection, so don't get confused if you don't see it. - Will present two ways on USMLE: <ol style="list-style-type: none"> 1) School-age kid (i.e., 12) who has coryza for a few days followed by petechiae and/or nosebleeds. 2) Woman 30s-40s + no mention of viral infection + random bruising + bleeding time 9 minutes. - For the latter vignette, if they say exact same Q but bleeding time 6 minutes (normal), then answer is domestic abuse, not ITP. - There is an unusual 2CK Q on new NBME where they say girl only has heavy menses (classically a clotting factor presentation for vWD) and the answer is ITP, but vWD isn't listed and the other answer choices are clearly wrong. Just letting you know this exists. - Tx = steroids, then IVIG, then splenectomy, in that order. - If splenectomy is performed and platelets return to normal range, but then 6 months later they fall again, the answer is "accessory spleen." Sounds weird, but a small % of people have a second spleen the size of a pea that can grow in size if the main spleen is removed.
vWD	<ul style="list-style-type: none"> - von Willebrand disease; autosomal dominant. - von Willebrand factor (vWF) normally bridges glycoprotein Ib on platelets to vascular endothelium / underlying collagen (platelet adhesion). - ↑ bleeding time; ↑ PTT (only half the time); no change PT; normal platelets. - ↓ vWF means ↓ platelet function (and hence ↑ BT), but platelet count is unchanged. - vWF also has secondary role of stabilizing factor VIII in plasma; since we have ↓ vWF, the intrinsic pathway gets fucked up, so we have ↑ PTT. But bear in mind, this effect on factor VIII <i>is only a mere secondary</i> role, so PTT isn't always ↑. It's to my observation that only ~50% of vWD vignettes give ↑ PTT. PT is normal because the extrinsic pathway is fine. - 8/10 Qs presents as a teenager or young adult with a mix of one platelet problem and one clotting factor problem. - Platelet problem = mild, cutaneous findings (i.e., petechiae, bruising) + epistaxis. - Clotting factor problem = excessive bleeding with tooth extraction + heavy menses. (Hemarthroses are also clotting factor but are seen in hemophilia, not vWD, as I explain below).

	<ul style="list-style-type: none"> - For example, the Q can give 17-year-old girl who has nosebleeds + heavy periods; or 17-year-old girl who has bruising + Hx of excessive bleeding with tooth extraction (i.e., we have one platelet problem + one clotting factor problem). This is 8/10 Qs I'd say. - 1/10 Qs might give only isolated platelet or clotting factor problem (i.e., only say the patient has Hx of excessive bleeding with tooth extraction), but they'll also say <i>one of the parents</i> has Hx of nosebleeds → so you say, "Oh ok. vWD is AD, so that's your combo of platelet problem + clotting factor problem linked via autosomal dominant inheritance." - 1/10 Qs will say the patient has a cut on the finger that takes longer to heal than normal + has heavy menses + normal platelets + has normal PT and PTT + they don't mention BT. The cut on the finger is their way of saying BT is elevated. Despite only an isolated ↑ in BT here, since platelets are normal, we know it's not ITP and is instead vWD. - Ristocetin cofactor assay is abnormal. All you need to know is that this is some test that is abnormal if platelet adhesion is fucked up. Tx = desmopressin (DDAVP), which can in theory help boost functional vWD levels.
Hemophilia A+B	<ul style="list-style-type: none"> - Deficiency of factors VIII and IX, respectively. - Both X-linked recessive. - Isolated ↑ PTT; BT and PT are normal. - Factors VIII and IX are in the intrinsic pathway, so PTT is ↑. Extrinsic pathway is unaffected so PT is normal. Platelets have nothing to do with this condition, which is why bleeding time is normal. - Will present two ways on USMLE: <ol style="list-style-type: none"> 1) School-age boy with hemarthrosis who has isolated ↑ PTT. They can also say he has a maternal uncle who died years ago from minor head trauma. 2) Neonate who has excessive bleeding with circumcision. - Hemophilia A is treated with DDAVP and factor VIII replacement. - Hemophilia B is treated with factor IX replacement. DDAVP doesn't work apparently. - If the Q tells you a patient with hemophilia A has persistently elevated PTT despite factor VIII supplementation, the answer is "check for antibodies against factor VIII." Sometimes patients can develop resistance against exogenous factor replacements.
Vitamin K deficiency	<ul style="list-style-type: none"> - Causes ↑ PT, ↑ PTT, no change bleeding time. - Vitamin K is cofactor for gamma-glutamyl carboxylase, which is an enzyme that activates clotting factors II, VII, IX, and X, as well as anti-clotting proteins C and S. - Bleeding time is normal because platelets aren't affected. - Will present two ways on USMLE: <ol style="list-style-type: none"> 1) Neonate who has bleeding from umbilical stump +/- retinal hemorrhages. The latter can sound like shaken-baby syndrome, but the bleeding from the umbilical stump is highly buzzy for vitamin K deficiency. 2) Adult who's been on broad-spectrum antibiotics for 6 weeks for, e.g., endocarditis, who now requires a lower dose of warfarin → answer = "depletion of bowel normal flora" (Vitamin K is normally synthesized by colonic normal flora). - Warfarin inhibits vitamin K function, so if Vit K is ↓, we don't need as much warfarin.
DIC	<ul style="list-style-type: none"> - Disseminated intravascular coagulation. - Runaway effect of clotting factor/platelet consumption, precipitated by multifarious etiologies such as trauma, sepsis, amniotic fluid embolism, and treatment of AML. - ↑ BT, ↑ PT, ↑ PTT, ↑ D-dimer, ↑ plasmin activity. - ↓ fibrinogen, ↓ platelets, ↓ clotting factors. - Fibrinogen decreased because it is converted to fibrin. - Plasmin breaks down fibrin, so more fibrin means more plasmin is upregulated in an attempt to dissolve it. - D-dimer = fibrin degradation products; since more fibrin is being broken down, fibrin degradation products (D-dimer) ↑. - "Bleeding from catheter/IV sites" is 9 times out of 10 synonymous with DIC. However on one 2CK Surg Q, dilutional thrombocytopenia secondary to ↑ blood transfusions presents the same. - Blood smear shows schistocytes.

	
HUS	<ul style="list-style-type: none"> - Hemolytic uremic syndrome. - Presents as triad of: 1) thrombocytopenia; 2) hemolytic anemia with schistocytes; and 3) renal insufficiency with or without hematuria. - The combination of thrombocytopenia + schistocytosis = microangiopathic hemolytic anemia (MAHA). - Mechanism is: E. coli (EHEC O157:H7) and Shigella both secrete toxins (Shiga-like toxin and Shiga toxin, respectively) that cause inflammation of renal microvasculature → ADAMTS13 protein inactivation → failure of cleavage of vWF multimers → platelet adherence to vascular endothelium cannot be as readily reversed → platelet aggregations protrude into vascular lumen causing shearing of RBCs flying past → fragmentation of RBCs (schistocytes, aka helmet cells).
TTP	<ul style="list-style-type: none"> - Thrombotic thrombocytopenic purpura. - Presents as HUS triad + fever and neurologic signs. In other words: - Presents as pentad of 1) thrombocytopenia; 2) schistocytes; 3) renal insufficiency; 4) fever; 5) neurologic signs. - TTP is caused by antibodies against, or a mutation in, a protein called ADAMTS13, which is a metalloproteinase that breaks down vWF multimers. - Can present as a stroke-like presentation in young woman, where they just want “schistocytes” as the answer. - 2CK NBME has “plasmapheresis” as Tx.
Sickle cell	 <ul style="list-style-type: none"> - Autosomal recessive; glutamic acid → valine missense mutation on the beta-chain. - Carrier status (one mutation) is referred to as sickle cell trait, which is less severe than sickle cell anemia (two mutations). - NBME wants “heterozygote advantage” as the basis for the existence of sickle cell – i.e., confers resistance to malaria. - Sickle cell crises can present as abdominal or chest pain, as well as dactylitis (inflammation of the fingers).

	<ul style="list-style-type: none"> - The abdominal pain, in particular, as the initial presentation for sickle crisis has become HY on NBME exams. A new 2CK form gives RLQ pain + low Hb in child from Libya, where "blood smear" is the answer for what will confirm the diagnosis. The Q is tricky because it almost sounds like appendicitis. - Diagnosed with blood smear, followed by hemoglobin electrophoresis to detect HbS. - Offline NBME Q asks which of the following best describes the molecular basis for sickling in a patient → answer = "gain of stabilizing hydrophobic interactions in the deoxygenated form of hemoglobin S." This is because valine is more hydrophobic than glutamic acid, so we have hydrophobic interactions enabling sickling. - Another NBME has "beta chain slips into a complimentary hydrophobic pocket on the alpha chain" as answer for sickling. - Sickling notably occurs with dehydration + increased acidity. This makes sense, since the surrounding environment would become less lipophilic, meaning the HbS would consolidate/collapse unto itself to minimize surrounding surface area contact. - Hydroxyurea ↑ HbF and can ↓ recurrence of sickle crises. Sounds weird, but the mere presence of more HbF simply means there's fractionally less HbS floating around.
Myelofibrosis	<ul style="list-style-type: none"> - Usually JAK2 mutation (same as polycythemia vera). - The answer on USMLE if they say "tear-drop-shaped RBCs" or "dry tap on bone marrow aspiration." - Massive splenomegaly seen in 100% of questions. - I've seen NBME also write "tear-drop shaped poikilocytes" (fancy word that means abnormal RBCs seen as >10% on a smear). - In myelofibrosis, the proliferation of abnormal cells in the bone marrow, notably megakaryocytes and granulocytes, leads to the release of growth factors and cytokines that stimulate deposition of collagen, resulting in bone marrow fibrosis.
Essential thrombocytosis (ET)	<ul style="list-style-type: none"> - Aka essential thrombocythemia. - Usually JAK2 mutation (same as myelofibrosis and polycythemia vera) causing over-proliferation of platelets. - USMLE Q will tell you patient has pain in fingertips, Raynaud phenomenon, or headache (hyperviscosity symptoms) + platelet count is, e.g., 1.4 million/μL (NR 150,000-450,000/μL). - ET is a myeloproliferative neoplasm where platelets can be >1,000,000/μL. - The patient will present with no specific triggering event. Compare this to reactive thrombocytosis below. - Tx = aspirin + plateletpheresis (removing platelets from blood).
Reactive thrombocytosis (RT)	<ul style="list-style-type: none"> - Aka reactive thrombocythemia. - Triggering event (i.e., inflammation, infection, surgery) can stimulate thrombopoietin production and increased synthesis and release of platelets. - It is to my observation the USMLE loves to give reactive thrombocytosis in the setting of infective endocarditis, where they'll tell you platelet count is 900,000, and the student is like, "why the fuck are the platelets 900,000." It's just RT. - ET is usually women >50 and is symptomatic; RT is anyone and is usually asymptomatic. When RT occurs, it will be a super-high platelet count you incidentally notice as part of the stem, but the focus of the Q isn't the patient's symptoms related to the ↑ platelets. - For example, there is a difficult offline NBME Q where they give neutrophilic shift with platelets of 1.4 million, where it looks like it could be RT due to infection (i.e., neutrophilic shift usually indicates bacterial infection), but the answer is ET on this form, not RT, presumably because the platelet count is >1 million (rare in RT to be this high) and the patient has symptoms (pain in fingertips). - Tx = address underlying infection + give aspirin. - I haven't seen RT as an actual correct answer on an NBME form; I've only seen it baked into questions as an incidental finding where the labs show high platelets in the setting of infection, and you, as the student, need to not be thrown off by that or think it's weird. You just say, "Oh that's probably just RT because we have infection/sepsis here."
Glanzmann	<ul style="list-style-type: none"> - Aka Glanzmann thrombasthenia. I've seen this on NBME as just "thrombasthenia." - Deficiency of glycoproteins IIb/IIIa on platelets → defective platelet aggregation.

Bernard-Soulier	<ul style="list-style-type: none"> - Deficiency of glycoprotein Ib on platelets → defective platelet adhesion. - Same as with vWD, has abnormal ristocetin cofactor assay.
SLE	<ul style="list-style-type: none"> - Systemic lupus erythematosus; classically women 20-40s. - Most common presenting feature is arthritis (>90%). - Malar rash too easy for most Qs, although you should know this is a type III HS. - Thrombocytopenia is mega-HY for Step – i.e., 32-year-old woman with arthritis + low platelets = SLE. - RBCs and WBCs can also be ↓, but it's the ↓ platelets that's highest yield. The cell lines are down due to antibodies. In other words, if you get a patient with SLE where all cell lines are down, this is due to "increased peripheral destruction," not "deficient bone marrow production." - Discoid lupus = skin lesions. Mucositis = mouth ulcers. - ↑ risk for malignancy (i.e., non-Hodgkin lymphoma) → i.e., 44-year-old woman with SLE has seizure + ring-enhancing lesion seen on CT of head → answer = primary CNS lymphoma; Toxo is wrong answer. - Causes diffuse proliferative glomerulonephritis, as discussed in HY Renal PDF. - SLE in pregnant women can cause congenital heart block in neonates. Sounds weird, but shows up on NBME somewhere. - Treat standard flares with steroids (i.e., prednisone).
PNH	<ul style="list-style-type: none"> - Paroxysmal nocturnal hemoglobinuria. - Red urine in patient waking up in the morning. - Mechanism is increased complement-mediated hemolysis caused by deficiency of CD55/59 + deficiency of GPI anchor, which protect RBCs from complement-mediated breakdown.
Hageman factor deficiency	<ul style="list-style-type: none"> - Hageman factor = factor XII, the first clotting factor in the intrinsic pathway. - All you need to know is that there is such thing as "Hageman factor deficiency" that presents as a completely asymptomatic/healthy adult who incidentally is discovered to have a ↑↑ PTT. - If factor XII is low, then XIIa will also be low, which means less pre-kallikrein is converted to kallikrein. - There is one retired NBME Q on it where the answer is "deficiency of kallikrein" in the setting of an asymptomatic 60-year-old dude who has mega ↑↑ PTT and Hageman factor deficiency. - You can call it dumb all you want. We're in agreement here. Doesn't change the fact it's on the NBME. Students have probably encountered the question not even realizing this is what they saw, hence first time you're hearing about this.

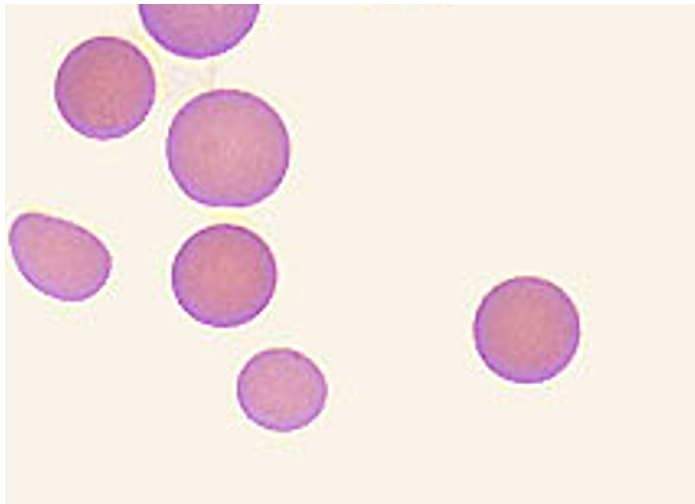
Thrombotic disorders	
Factor V Leiden	<ul style="list-style-type: none"> - Just be aware that there is a condition called FVL, which means the patient will have ↑ clots / DVTs. - Normally factor Va and VIIIa are reversed to V and VIII by protein C (protein S is a cofactor for protein C). In FVL, we have "activated protein C resistance," which means Factor V is resistant to cleavage by protein C. - Conditions such as Prothrombin mutation and MTHFR also cause ↑ clots, but are lower yield.
Protein C deficiency	<ul style="list-style-type: none"> - Causes clots/DVT, same as FVL, but is notably associated with skin necrosis if the patient receives warfarin.
Antithrombin III deficiency	<ul style="list-style-type: none"> - AT III is required to reverse IIa (thrombin), Xa, and IXa back to inactive II, X, IX. - Presents two ways on USMLE: <ol style="list-style-type: none"> 1) Young, otherwise healthy adult who has thromboses + the Q mentions nothing about PT or PTT. 2) Patient with nephrotic syndrome who has DVT, superficial thrombophlebitis, renal vein thrombosis, or varicocele. AT III is a protein that can be lost in the urine.

Antiphospholipid syndrome (APS)	<ul style="list-style-type: none"> - Antibodies against phospholipids that cause <i>in vivo</i> thromboses despite a paradoxical <i>in vitro</i> ↑ PTT (i.e., if PTT is ↑, you'd think we'd have bleeding diathesis, not thromboses). - PTT is fucked up because we need phospholipids for the <i>in vitro</i> assay to work. - <i>In vivo</i>, we have thromboses however because 1) antibodies against phospholipids in platelet membranes activate platelets and cause them to secrete procoagulant molecules; 2) these antibodies also bind to vascular endothelial cells, causing endothelial dysfunction and prothrombotic state; 3) the antibodies are pro-inflammatory, where ↑ activity of IL-6 and TNF-α activates tissue factor (factor III). USMLE WILL NOT assess you on these three mechanisms; I merely write them here because this diagnosis is exceedingly HY but remains perennially elusive and confusing as fuck for students. - Can be idiopathic (i.e., caused by antibodies against β₂-microglobulin or cardiolipin), or secondary to SLE. - If APS is due to SLE, we merely call these antibodies "lupus anticoagulant," but they're the same antibodies. - For whatever magical reason, APS can cause false(+) VDRL syphilis tests.
---------------------------------	--

HY Neutropenia conditions	
<ul style="list-style-type: none"> - A HY general point for USMLE is that neutropenia can present as mouth ulcers, fever, and sore throat. - Questions will not usually come out and say, "Yes, the kid has neutropenia." The situation might be, e.g., a kid who's undergoing chemotherapy for AML who now has mouth ulcers and/or sore throat. 	
Neutropenic fever (Febrile neutropenia)	<ul style="list-style-type: none"> - Neutropenia + fever, LOL! - Can occur in the setting of patient who has chemo- or radiotherapy-induced pancytopenia (i.e., RBCs, WBCs, and platelets are all ↓), or viral-induced neutropenia (i.e., Parvovirus B19), where you see that the patient has fever and neutrophils are low (+/- RBCs and platelets). - Medical emergency (i.e., the patient has infection but no ability to fight it). USMLE wants "IV broad-spectrum antibiotics" as the next best step. - After Abx, the USMLE wants granulocyte colony-stimulating factor (i.e., G-CSF, or filgrastim) as the answer. - I've never seen granulocyte transfusion as a correct answer on USMLE.
Viral-induced neutropenia	<ul style="list-style-type: none"> - Parvovirus B19 can infect myeloid precursors and cause neutropenia – i.e., viral-induced neutropenia. - Other viruses can cause formation of antibodies against neutrophils, similar to how they can cause antibodies against platelets in ITP.
Cyclic neutropenia	<ul style="list-style-type: none"> - Gene mutation causing episodes of fever + mouth ulcers in a kid age 1-3. These episodes typically occur every 21 days, but the Q might not specify this number and will just say, "There have been several episodes like this before."

Other anemias	
Aplastic anemia	<ul style="list-style-type: none"> - Means all cell lines (i.e., RBCs, WBCs, platelets) are ↓. - Can be due to Parvo B19, where it infects not just myeloid progenitors, causing neutropenia, but also erythroid progenitors and megakaryocytes, causing ↓ RBCs and platelets, respectively. - Can also be due to other viruses, such as HepA CMS Peds 5) or HIV (Free 120). - Can be chemo- and/or radiotherapy-induced. - Fanconi anemia is rare, AR aplastic anemia that, for whatever reason, also presents with hypo-/aplastic thumbs/radii.
Pure-RBC aplasia	<ul style="list-style-type: none"> - Means only RBCs are ↓. - Can be caused by Parvo B19. - Thymoma can cause pure-RBC aplasia (as well as myasthenia gravis).

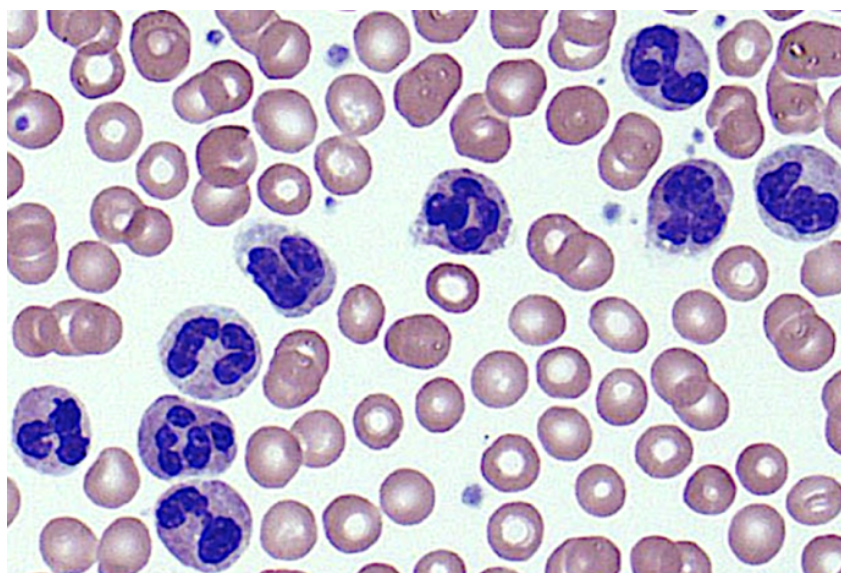
	- Diamond-Blackfan anemia is rare pure-RBC aplasia that presents with triphalangeal thumbs.
--	---

Spherocytosis	
Hereditary	<ul style="list-style-type: none"> - Autosomal dominant (one of the highest yield inheritance patterns on USMLE). - Heterozygous mutation in ankyrin, spectrin, or band proteins, causing an RBC cell membrane/cytoskeletal defect. This causes the RBC to deform away from the normal biconcave disc and into a spherical shape. - The USMLE might give you hereditary spherocytosis and then the answer is just "cell membrane," or "cytoskeleton," or "cytoskeletal defect." - Can be described as RBCs lacking central pallor. If they show you a smear, they look full and red.  <ul style="list-style-type: none"> - Causes a normochromic, normocytic anemia (asked on an NBME directly). - Can cause pigment stone cholelithiasis due to the spleen identifying the spherocytes as abnormal and increasing RBC turnover. - RBC mean corpuscular hemoglobin concentration (MCHC) can be \uparrow. This is not specific to spherocytosis but is nevertheless a rare lab parameter to see in Qs. It's to my observation that if they mention it, 4/5 times the Dx is spherocytosis. - Diagnose via osmotic fragility test and eosin-5-maleimide. - Coombs test is negative (meaning we don't have antibodies against RBCs). This is important in terms of contrasting with spherocytosis due to hemolysis (as I discuss below). - Treatment is splenectomy (to \downarrow RBC turnover). The answer can appear on USMLE as "splenectomy and cholecystectomy" together. - USMLE can mention a child who has a low Hb + one of the parents had splenectomy +/- cholecystectomy performed in the past for "an anemia" \rightarrow answer = hereditary spherocytosis. I also point out to the student the AD inheritance pattern based on one of the parents having the condition as well. - Q can also just ask straight-up which heme condition is often treated with splenectomy, and the answer is hereditary spherocytosis; students sometimes erroneously choose sickle cell. Remember, sickle cells causes autosplenectomy due to repeated microinfarcts within splenic microvasculature; it is not treated with splenectomy.
Hemolytic anemia	- Spherocytosis is not always due to hereditary spherocytosis and can sometimes be seen with drug- or infection-induced hemolysis.

	<ul style="list-style-type: none"> - In this case, the Coombs test is (+), meaning we have antibodies against RBCs. In contrast, with hereditary spherocytosis, the mechanism has nothing to do with antibodies, so Coombs test is (-). - Antibodies binding to RBCs can trigger complement-mediated damage, which can lead to deformation of the RBC membrane and cytoskeleton. - USMLE will give kid with recent viral infection who has low Hb and spherocytes on a smear + positive Coombs; answer = hemolytic anemia, not hereditary spherocytosis (i.e., answer = "no specific mutation").
--	---

Leukemoid reaction

- Exaggerated immune response to infection in which WBCs go $\uparrow\uparrow$ and can hence resemble leukemia.
- As I mentioned before, "-oid" means "looks like but ain't," so the patient's lab can look like leukemia (because the WBCs are so high), but it's not leukemia.
- Normal leukocyte count is 4-11,000/ μ L. Typical infections might cause WBCs to go \uparrow to the teens or 20,000s/ μ L. But when WBC levels creep into the 30s, this becomes increasingly rare, even for patients who are septic, so we want to start thinking about leukemia. This is why if the patient doesn't turn out to have leukemia we call it leukemoid reaction.
- This will be the answer on USMLE for patient who has **infection + WBCs >30,000/ μ L, PLUS** they give you a blood smear that shows neutrophils or they say leukocyte ALP is elevated (in CML it's low).

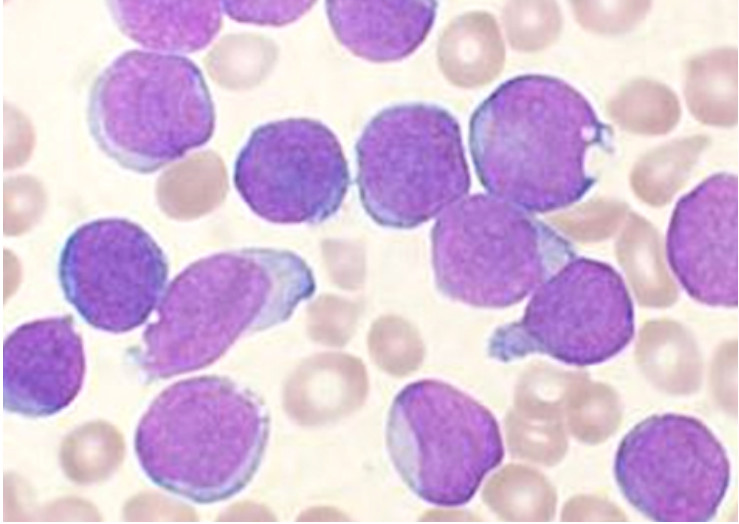
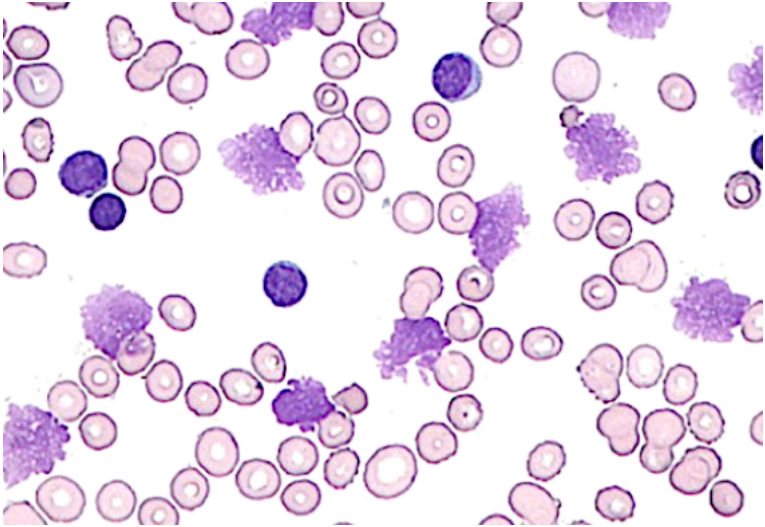


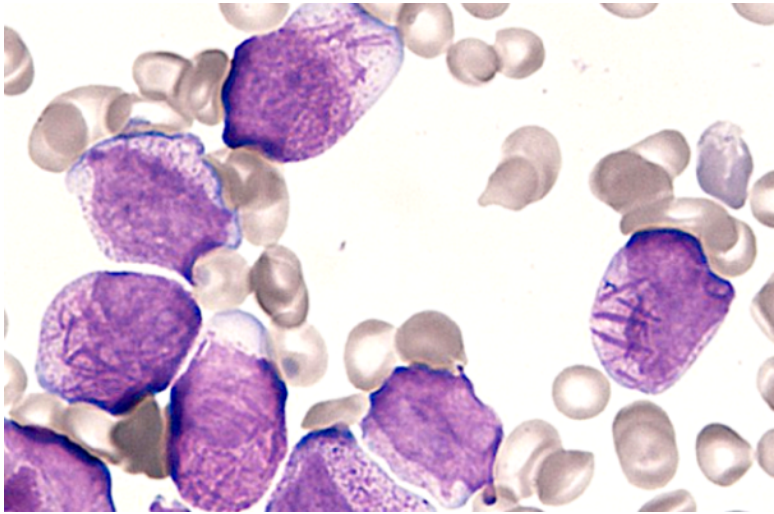
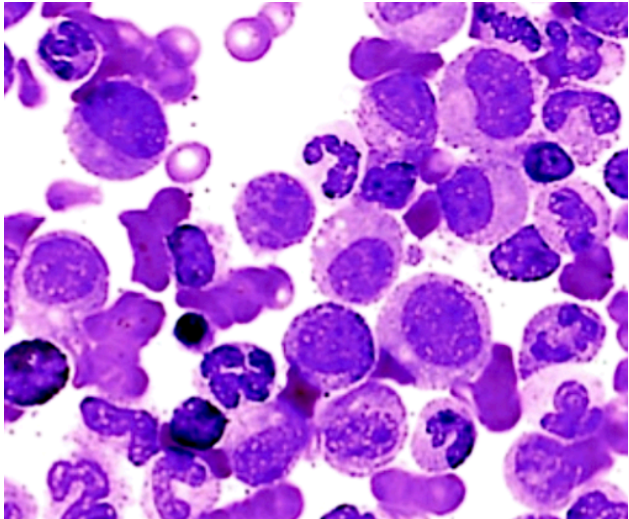
- This is the smear the USMLE will show you if they want leukemoid reaction. This is showing you **neutrophilia** (i.e., just lots of neutrophils). They can also write the answer as **reactive granulocytosis**, or as "increased release of leukocytes from bone marrow post-mitotic reserve pool."
- A typical leukemoid reaction Q might give you a UTI + WBCs 32,000/ μ L + the above smear. Not hard.

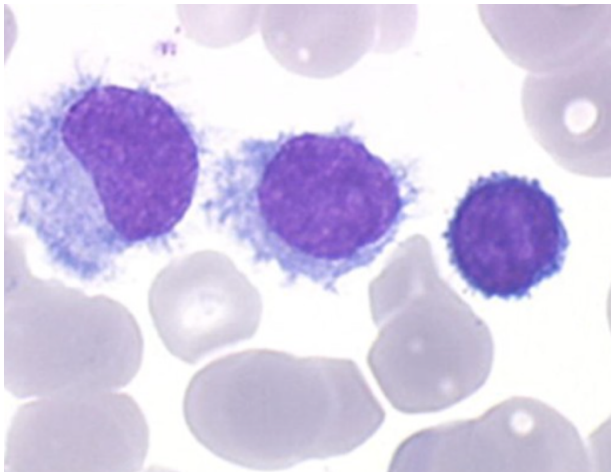

HY Leukemias

- A leukemia is a cancer of white blood cells in the blood.
- They are almost always B-cell in origin.
- Apart from Sezary syndrome and mycosis fungoides (discussed below), if one of the HY lymphocytic leukemias (i.e., ALL, CLL) is T-cell in origin, USMLE will give an SVC-like syndrome (i.e., positive Pemberton sign with congested neck veins and/or facial erythema/swelling) due to a thymic lesion.

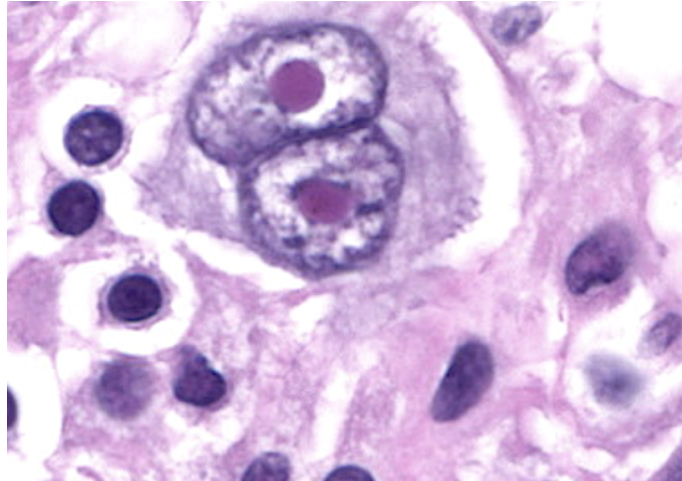
ALL	<ul style="list-style-type: none"> - Acute lymphoblastic leukemia. - The answer on USMLE for a kid with leukemia (i.e., pre-adolescent).
-----	--

	<ul style="list-style-type: none"> - Q will give you kid who's, e.g., 6-years-old, and has leukocyte count of 60,000/μL, where it's 90% lymphocytes. - An important DDX of ALL is pertussis, that for whatever reason, can cause an ALL-like picture where WBCs can be 30-40,000+, where it's 90% lymphocytes. This is called reactive lymphocytosis. The distinction with ALL is that, in pertussis, they'll say there's a cough and/or post-tussive emesis (vomiting after cough) and/or hypoglycemia (HY finding in pertussis). - ALL can be CD10 and TdT positive. Dumb, but I've received feedback of them showing up. - \uparrow Risk with Down syndrome. The Q can give you standard vignette of Downs and then ask for what child is at greatest risk of developing \rightarrow answer = "excess lymphoblasts."  <p>ALL; lymphoblasts appear smooth and relatively uniform.</p>
CLL	<ul style="list-style-type: none"> - Chronic lymphocytic leukemia. - Vignette will sound just like ALL but not in a kid (usually older adults). - The Q might say 70-year-old + WBCs 87,000/μL (90% lymphocytes), where they ask for the next best step \rightarrow answer = "quantitative immunoglobulin assay," which can show \uparrow monoclonal immunoglobulin sometimes in CLL. Sounds nitpicky, but it's an answer on an NBME. - CLL smear can show smudge cells, which are fragile cells on LM.  <ul style="list-style-type: none"> - Leukemic cells are CD5 and CD23 positive (asked on an NBME). - Can be associated with warm autoimmune hemolytic anemia (IgG against RBCs).

AML	<ul style="list-style-type: none"> - Acute myeloblastic leukemia. - Will show Auer rods on a smear.  <ul style="list-style-type: none"> - The image of Auer rods is exceedingly HY for the Step. They are composed of myeloperoxidase, which is a blue-green heme-containing pigment. - If an AML Q doesn't give you the buzzy image of Auer rods, they'll say there's "30% blasts" or "50% blasts." - Acute promyelocytic leukemia (APL; aka AML type M3) has a t(15;17) translocation. - Tx is all-<i>trans</i> retinoic acid (vitamin A). This causes the maturation of leukemic cells into mature granulocytes. - Tx of AML also leads to leukemic cell lysis, where release of Auer rods into the circulation can precipitate DIC.
CML	<ul style="list-style-type: none"> - Chronic myelogenous leukemia. - Caused by t(9;22) translocation (Philadelphia chromosome). - Results in formation of bcr/abl tyrosine oncogenic tyrosine kinase, which is a "fusion protein." - The stem will say there's all sorts of myelo-sounding cells – i.e., myelocytes, promyelocytes, metamyelocytes. 9/10 Qs that mention these cells are CML. - Leukocyte ALP is low. - Smear shows what I refer to as a "motley mix" or "soup," which shows all different types of cells. 

	<ul style="list-style-type: none"> - This is HY smear that differentiates it from leukemoid reaction (which instead shows neutrophilia). - Tx is with imatinib, which targets the bcr/abl tyrosine kinase.
Hairy cell	<ul style="list-style-type: none"> - Q will merely say patient has leukemia characterized by "cytoplasmic projections" that stains positive for tartrate-resistant acid phosphatase (TRAP).  <ul style="list-style-type: none"> - The stem can give low WBCs, which is unusual for leukemia. 9 out of 10 questions for leukemia will give ultra-HY WBCs. The NBME Q I've seen on hairy cell gives image similar to above + gives WBCs 3,500 + they say WBCs with cytoplasmic projections" + stains positive for TRAP.
Sezary Syndrome	<ul style="list-style-type: none"> - Cutaneous T-cell lymphoma that extends to the blood as a T-cell leukemia. - Caused by human T-cell lymphotropic virus (HTLV). - Has cerebriform-shaped T cells in blood stream.  <ul style="list-style-type: none"> - Presents classically as erythroderma (red skin).

Lymphomas	
	<ul style="list-style-type: none"> - A lymphoma is a cancer of the lymphatic system. - Usually starts in lymph nodes, but can also be present in other areas of the lymphatic system, such as the spleen and bone marrow. - Almost always B-cell in origin. - Lymphomas are categorized as Hodgkin or non-Hodgkin (NHL). - Epstein-Barr virus, HIV, general immunosuppression (i.e., chronic corticosteroids or immunosuppressant drugs), and autoimmune disease (e.g., SLE, Hashimoto) increase the risk for lymphomas.
Hodgkin	<ul style="list-style-type: none"> - Characterized by Reed-Sternberg cells, which are CD15/30 (+) B cells with a characteristic "owl eye" appearance.



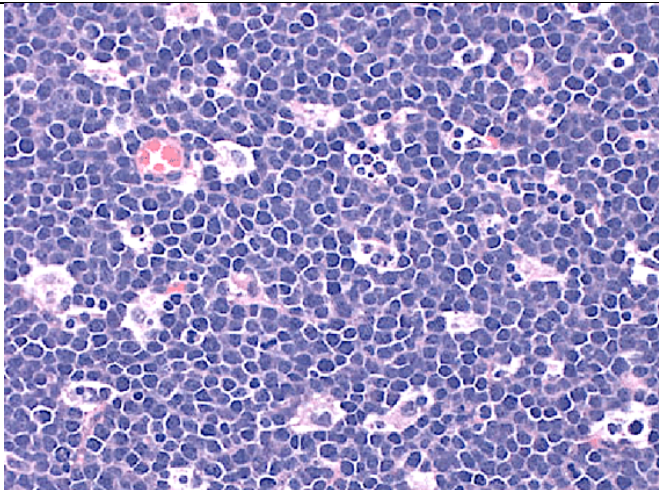

- 100% of questions give a painless lateral neck mass or facial swelling (lymphadenopathy).
- The USMLE Q will then give at least one additional finding of: 1) hepatomegaly; 2) mediastinal mass (not thymoma; this is mediastinal lymphadenopathy); 3) Virchow node (Troisier sign of malignancy; palpable left supraclavicular lymph node); this is not limited to gastric cancers; I've seen an NBME Q where they give this latter finding for Hodgkin.
- B symptoms (i.e., fever, night sweats, weight loss) are common but not mandatory in vignettes.
- Question can give normal leukocyte count and differential. An NBME Q gives WBCs of 10,000/ μ L (NR 4-11,000) and lymphocytes of 33% (NR 25-33). This is because lymphomas are cancers of lymphatic tissue. They're not leukemias, which are cancerous WBCs floating around the blood.
- Nodular-sclerosing type tends to favor women.
- \uparrow Normal B cells relative to abnormal RS cells = better prognosis. For example, leukocyte-rich Hodgkin has \uparrow normal B cells in comparison to RS cells and has better prognosis; in contrast, leukocyte-deplete Hodgkin has comparatively more RS cells and worse prognosis.

Burkitt



- t(8;14) translocation of c-myc gene; can rarely be t(2;8) or t(8;22).
- c-myc is a transcription factor.
- Presents classically as jaw lesion in African boy, or as abdominal lesion.

- Histo is buzzy "starry sky" appearance, which is a background of basophilic (purple) B cells with translucent macrophages.

	 <p>- Sounds odd, but NBME wants you to know the macrophages are called “tingible body” macrophages (not tangible), which phagocytose the lymphomatous B cells undergoing apoptosis. An NBME Q points to a tingible body macrophage and then the answer is just “apoptosis.” The macrophage itself isn’t undergoing apoptosis; it’s merely phagocytosing the apoptotic B cells characteristic of Burkitt. You might ask, “If the B cells are undergoing apoptosis, then how is the cancer growing/spreading?” The answer is that the rate of proliferation far exceeds that of the apoptosis.</p>
Follicular	<ul style="list-style-type: none"> - t(14;18) translocation of <i>Bcl-2</i> gene, which codes for an anti-apoptotic molecule. - Most common indolent NHL (which means less aggressive). - Presents as waxing/waning painless neck mass over 1-2 years.
DLBCL	<ul style="list-style-type: none"> - Diffuse large B cell lymphoma. - Most common aggressive NHL.
Mantle cell	<ul style="list-style-type: none"> - t(11;14) translocation involving over-expression of cyclin D → can’t halt cell cycle.
Mycosis fungoides	<ul style="list-style-type: none"> - Cutaneous T-cell lymphoma characterized by cerebriform-shaped cells. - Less aggressive than the T-cell lymphoma of Sezary syndrome and does not extend to the blood as a T-cell leukemia.  <p>- An important differential for “skin rash.”</p>

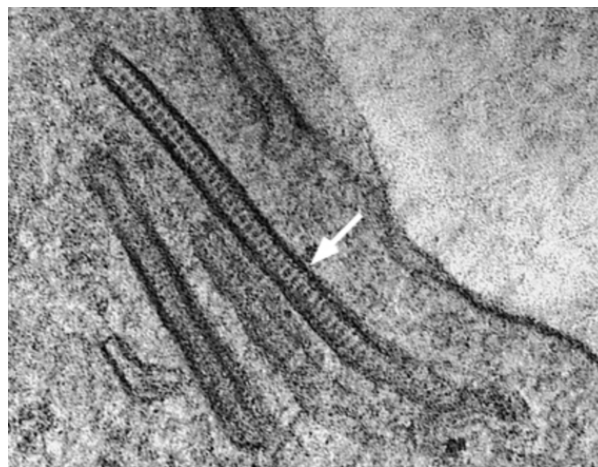
Warm vs cold autoimmune hemolytic anemia (AIHA)	
<ul style="list-style-type: none"> - Both present with (+) Coombs test, which just means antibodies against RBCs. - In other words, if a Q says Coombs is (+), we have Abs against RBCs; if it's (-), we don't. 	
Warm	<ul style="list-style-type: none"> - IgG antibodies against RBCs. - "Warm" because agglutination of RBCs occurs at warmer temperatures. The stem can say agglutination occurs when the nurse holds the tube of blood by hand. - Seen on USMLE for autoimmune diseases like SLE or RA; CLL; or can be drug- or infection-induced.
Cold	<ul style="list-style-type: none"> - IgM antibodies against RBCs. - "Cold" because agglutination of RBCs occurs at cooler temperatures. The stem can say agglutination occurs while the tubes are transported en route to the laboratory. - Seen on USMLE for <i>Mycoplasma pneumonia</i> and CMV mononucleosis.

Infectious mononucleosis
<ul style="list-style-type: none"> - Usually caused by EBV, but can also be CMV. - The virus invades B cells, which then stimulates the immune system to produce CD8+ T cells attacking the viral-infected B cells. In mono, these CD8+ T cells are called "atypical lymphocytes." The USMLE wants you to know these are reactive CD8+ T cells. They are "reactive" because they are responding to the viral-infected B cells. - Primary infection presents usually in teenager or young adult with fever >38 C, lymphadenopathy, tonsillar exudates, and lack of cough, making the presentation appear bacterial (in the HY Pulmonary PDF, I talk about CENTOR criteria for differentiating bacterial from viral URTIs). As a result, it is often misdiagnosed as <i>Strep</i> pharyngitis. - If amoxicillin or penicillin is given to treat EBV, this can cause a rash. This is not to be confused with a rash caused by allergy to beta-lactams. If pre-adolescent receives beta-lactam and gets a rash, that is likely beta-lactam allergy. If a patient adolescent or older gets a rash, we do a heterophile antibody (Monospot) test as next best step in diagnosis, as EBV mono is more likely. - Following the primary infection, mono can present as recurrent episodes of extreme fatigue that arise at interval-separations of months to years.

Langerhans cell histiocytosis (LCH)
<ul style="list-style-type: none"> - Overproduction of Langerhans cells, which are the dendritic cell of the skin. A dendritic cell is a strict antigen-presenting cell (APC), which phagocytosis antigen, migrates to lymph nodes and the spleen, and presents it to CD4+ T cells. Macrophages and B-cells are also APCs, but they are not dendritic cells because they have additional functions – i.e., macrophages destroy antigens; B cells mature into plasma cells and produce antibodies. - The Langerhans cells that over-proliferate do so notably in bone, causing lytic lesions (e.g., of the skull). - Birbeck granules are tennis racquet- or rod-shaped inclusions within the Langerhans cells, visualized on electron microscopy. Students remember the granules are tennis racquet-shaped, but don't know the rod-shape. There is an LCH Q on NBME where they give the rod-shaped Birbeck granules, and students are confused because they say, "But wait, they're not tennis racquet-shaped though."

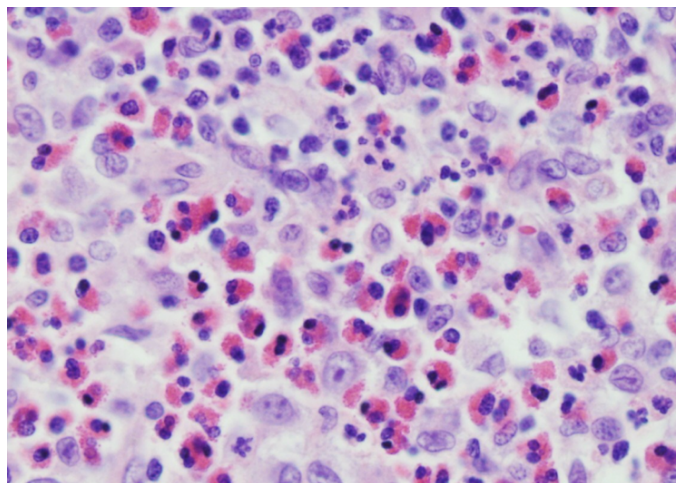


Tennis racquet-shaped Birbeck granules.



Rod-shaped Birbeck granules.

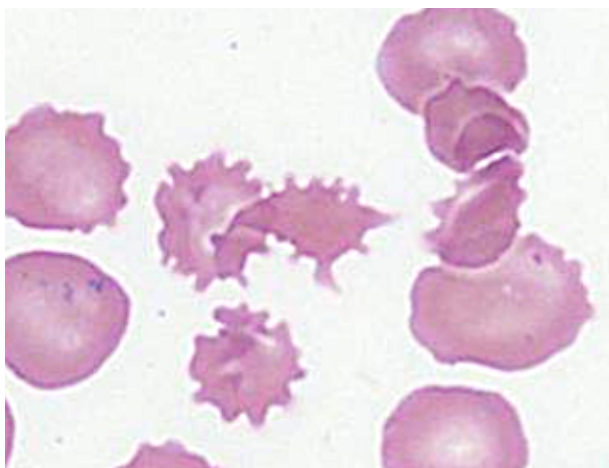
- There is difficult LCH NBME Q floating around where they don't show the Birbeck granules at all and instead just show the abnormal Langerhans cells straight-up. They will tell you a kid has a lytic lesion of his skull and then they show you image similar to the following:



- You say, "No idea what I'm looking at." Agreed. But it's on the NBME. Apparently the Langerhans cells in LCH appear as large, irregularly shaped cells with copious eosinophilic cytoplasm and characteristic horseshoe- or kidney-shaped nuclei.

Acanthocytes (spur cells)

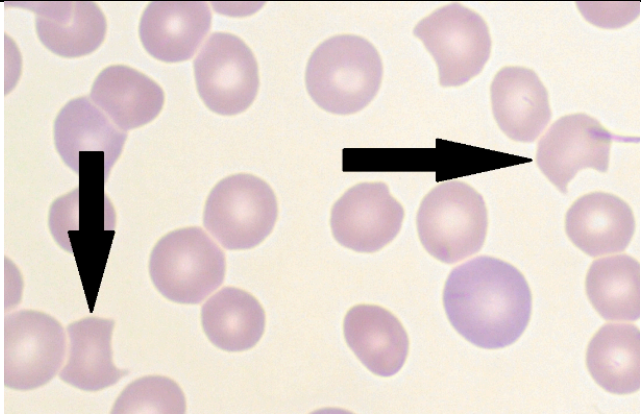
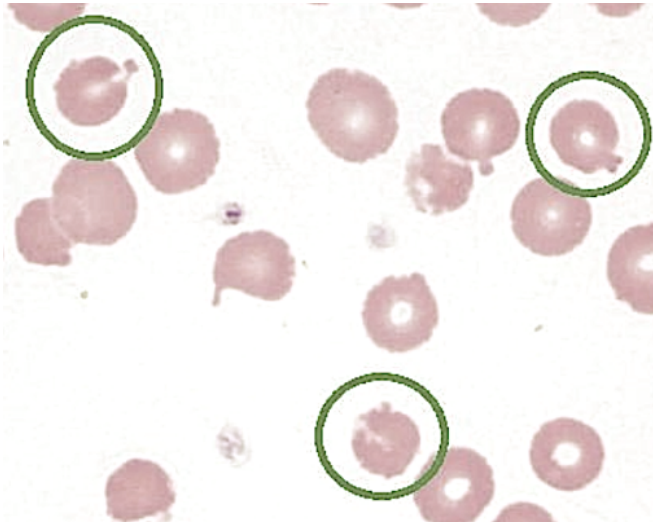
- Spiky RBCs that show up notably in **liver failure due to heat stroke**.
- I've probably only seen around 4 questions with acanthocytes on NBME material ever. 3 out of 4 are liver failure; 1 out of 4 is abetalipoproteinemia. Other resources get the yieldness reversed, where they mention abetalipoproteinemia as though it's this HY association. Nonsense. USMLE cares about liver failure.
- **Heat stroke** is end-organ damage due to hyperthermia (>104 F); heat exhaustion is mere fatigue with no end-organ damage due to hyperthermia. Heat stroke presents on Qs as abnormal liver and/or renal function tests.
- Q will say old lady found in her house in the summer has body temp of 106 F and acanthocytes on a blood smear; what's the diagnosis? → answer = liver failure (due to heat stroke).
- Another NBME Q gives hepatitis C patient with acanthocytes. The latter aren't critical to answer the Q, but I noted that the NBME mentioned them for hepatitis (i.e., not just heat stroke).



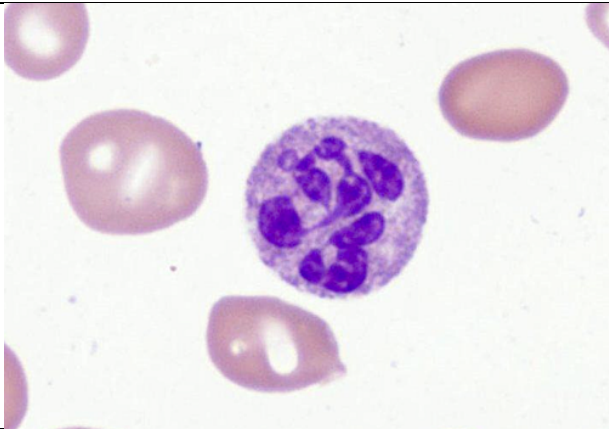
G6PD + PK deficiencies

G6PD deficiency

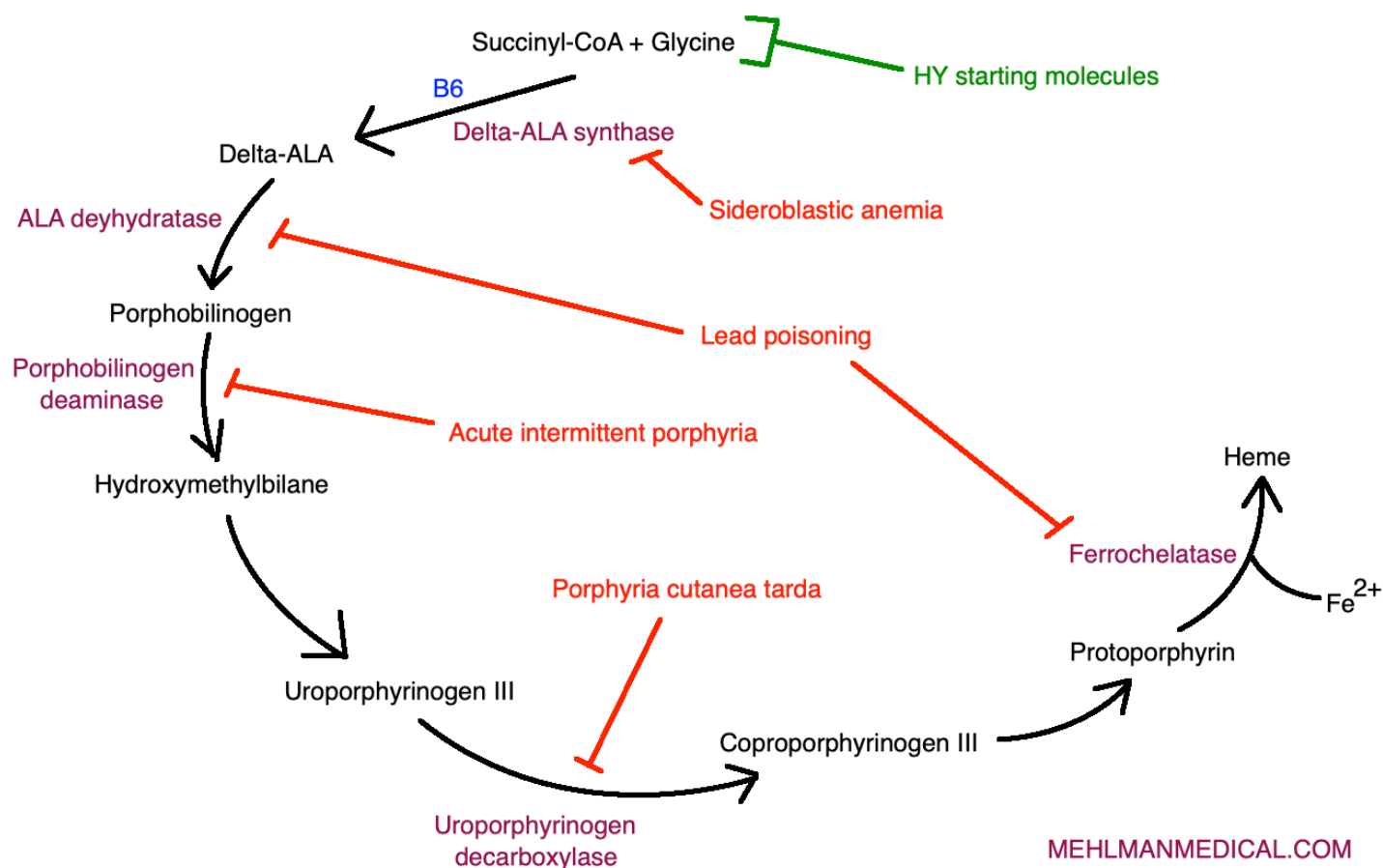
- Glucose-6-phosphate dehydrogenase deficiency; **X-linked recessive**.
- Most common cause of hemolysis due to an enzyme deficiency.
- Presents as hemolysis and jaundice in boy who recently received a drug or had a viral infection.
- HY agents that can precipitate oxidative damage of RBCs in G6PD are primaquine, dapsone, and sulfa drugs, and fava beans.
- Vignette might be 12-year-old boy with scleral icterus following a viral infection. Labs might show increased unconjugated hyperbilirubinemia and LDH (due to hemolysis). RBCs are packed with LDH. High LDH can be the USMLE's way of saying there is hemolysis.
- G6PD is an enzyme necessary to produce NADPH, which is a reducing agent that protects RBC membranes from oxidative damage.
- Bite cells and Heinz bodies are buzzy and HY. Bite cells are RBCs with bite-like notches caused by oxidative damage. Heinz bodies are clumps of oxidized/denatured hemoglobin.

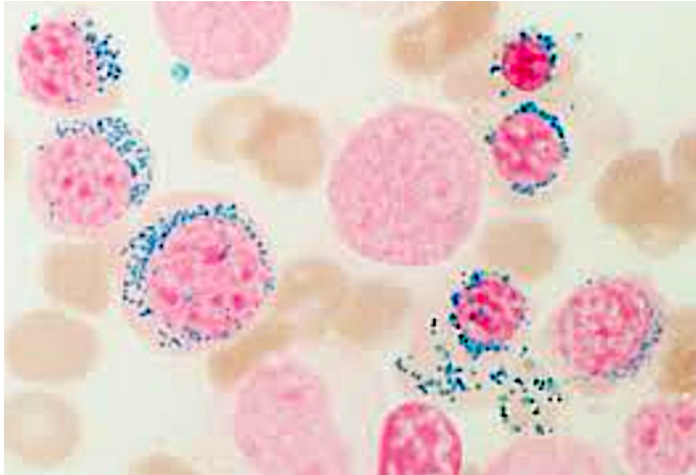
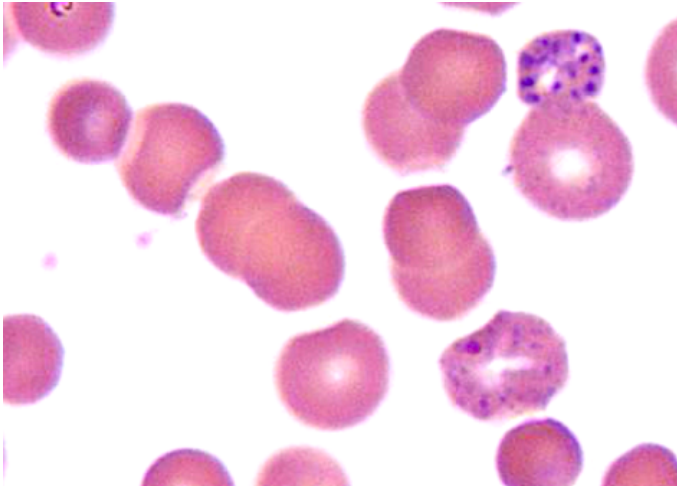
	 <p>Bite cells</p>  <p>Heinz bodies</p>
Pyruvate kinase	<ul style="list-style-type: none"> - Second most common cause of hemolysis due to an enzyme deficiency. - Leads to ↓ ATP production → ↓ activity of RBC Na/K-ATPase pumps → ↓ Na⁺ pumped out of RBC → water stays with Na⁺ → cellular swelling + lysis.

Macrocytosis causes	
<ul style="list-style-type: none"> - Normal RBC mean corpuscular volume (MCV) is 80-100 fL (femtoliters). - Macrocytosis refers to large RBCs (>100 fL). 	
B9 (folate) / B12 deficiencies	<ul style="list-style-type: none"> - Deficiency of either vitamin leads to impaired DNA synthesis, where RBCs remain in the bone marrow for a longer time period, leading to RBCs that are larger and less mature. - High MCV as a result of impaired DNA synthesis is called megaloblastic anemia. - Impaired DNA synthesis also causes hypersegmented neutrophils, where longer time spent in the bone marrow results in an increased number of nuclear lobes and segments.

	
Alcohol	<ul style="list-style-type: none"> - An important cause of high MCV on USMLE in the setting of normal B9/B12 levels. - Alcohol can also cause other types of anemia (i.e., sideroblastic).
Orotic aciduria	<ul style="list-style-type: none"> - Obscure condition where DNA synthesis gets impaired, leading to increase in MCV. - Can be caused by various enzyme deficiencies. - Maybe shows up in one NBME Q in all of history. You could just peripherally be aware it's a rare as fuck cause of high MCV. - Leflunomide, an obscure drug used for rheumatoid arthritis, inhibits dihydroorotate dehydrogenase, one of the enzymes that's deficient in orotic aciduria.

Heme synthesis + disorders



Heme synthesis disorders	
Sideroblastic anemia	<ul style="list-style-type: none"> - Impaired first step of heme synthesis (i.e., succinyl-CoA + glycine, via B6 and δ-ALA synthase \rightarrow δ-ALA) due to deficiency or impairment of δ-ALA synthase. - Can be X-linked recessive, but also can be caused by alcohol. - Failure to incorporate iron into heme. This leads to "ringed sideroblasts," which are erythroblasts (RBC precursors) where iron accumulates inside the mitochondria, where the latter form a ring around the nucleus. - The iron-laden macrophages stain blue with Prussian blue stain, making this a very buzzy and pass-level image for USMLE. 
Lead poisoning	<ul style="list-style-type: none"> - USMLE wants you to know lead inhibits both δ-ALA dehydratase and ferrochelatase. - Results in buildup of δ-ALA. - The stereotypical vignette of a 2-year-old eating paint chips in an old house leading to mental deterioration is too easy and maybe only $\sim 1/3$ of lead questions. - The other $2/3$ will be an adult who has microcytic anemia and mental decline. Buzzy hobbies can be hunting (bullets containing lead) or home-brewing of alcohol (casks made of lead).  <ul style="list-style-type: none"> - Can cause basophilic stippling of RBCs (rRNA precipitates). - Tx is calcium EDTA, dimercaprol, or succimer.
AIP	<ul style="list-style-type: none"> - Acute intermittent porphyria. - Autosomal dominant (sounds LY, but asked straight-up on an offline NBME somewhere). - Caused by deficiency of porphobilinogen deaminase (asked on NBME); causes buildup of porphobilinogen and δ-ALA. - Answer on USMLE for the heme synthesis disorder where patient has red/pink/port wine colored urine and abdominal pain.

	<ul style="list-style-type: none"> - Patients can sometimes have miscellaneous neurologic findings, but not mandatory. - Treatment is hematin and glucose.
PCT	<ul style="list-style-type: none"> - Porphyria cutanea tarda. - Caused by deficiency of uroporphyrinogen decarboxylase, leading to increased urinary uroporphyrins. - Answer on USMLE for the heme synthesis disorder where patient has photosensitivity / blistering. - Urine can appear "tea-colored" / dark. Don't confuse this with the red/pink/port wine colored urine in AIP.

Intra- vs extra-vascular hemolysis	
Intravascular	<ul style="list-style-type: none"> - Lysis of RBCs within the bloodstream. - Causes release of bilirubin directly into the blood, leading to hemoglobinuria. - Serum haptoglobin is decreased. Haptoglobin is a protein produced by the liver that binds to and removes free hemoglobin released from damaged or lysed RBCs. This mopping up of hemoglobin by haptoglobin prevents renal damage and helps to recycle iron. Low serum haptoglobin levels can be used to differentiate intra- from extra-vascular hemolysis). - A few HY examples of intravascular hemolysis are: <ul style="list-style-type: none"> - a) G6PD deficiency (oxidative damage to RBCs). - 2) PNH, due to complement-mediated hemolysis; - 3) HUS, TTP, HELLP syndrome, DIC, mechanical hemolysis by prosthetic valves due to shearing of RBCs (all schistocytes).
Extravascular	<ul style="list-style-type: none"> - Phagocytosis and lysis of RBCs within the spleen (and also liver). - Hemoglobin from lysed RBCs is not released directly into the bloodstream; it is broken down within macrophages, forming biliverdin, which is converted to bilirubin. Bilirubin then goes to the liver for excretion in bile. - There is no hemoglobinuria. - Haptoglobin is not decreased. - HY examples are: <ol style="list-style-type: none"> 1) Hereditary spherocytosis (abnormal shape leads to clearance by spleen). 2) Thalassemias (imbalanced Hb chains leads to RBC structural imbalance, which is recognized by the spleen as defective RBCs). 3) Warm and cold AIHA, where Abs opsonize RBCs, leading to their removal in red pulp of the spleen. (It should be noted that Abs in AIHA can also lead to intra-vascular hemolysis if complement is recruited, but most destruction of RBCs in AIHA is extra-vascular.)

Hemolytic disease of newborn types	
Rhesus (Rh) type	<ul style="list-style-type: none"> - ~85% of people have Rh antigen on their RBCs – i.e., Rh(+). Women who are in the ~15% that are Rh(-) are at risk of developing IgG antibodies against Rh antigen if the fetus is Rh(+) and the circulations mix inadvertently. - When the mother develops antibodies against Rh (i.e., has become sensitized to it), we call this "Rh isoimmunization." NBME will throw this word around a bit, so you need to know it means "she's developed IgG antibodies against Rh." - Mechanism: Rh(-) mom in first pregnancy is exposed to fetal blood that is Rh(+); mom makes Abs against Rh; subsequent pregnancy results in IgG against Rh crossing placenta and targeting fetal Rh(+) RBCs, leading to hemolysis in the fetus.

	<ul style="list-style-type: none"> - As mentioned earlier, Rh status is checked at the first antenatal screening at 8-10 weeks. If the mother is Rh(-), then give RhoGAM at 28 weeks as well as at parturition. It must also be given if there are any interventions (e.g., amniocentesis), or if there's complications like spontaneous abortion or abruptio placentae. - If 2nd pregnancy onward, if Rh (-) woman is found to have titers against Rh, do not give RhoGAM during the pregnancy, since it's too late. - Kleihauer-Betke (KB) test is done in setting of hemorrhage or suspected mixing of maternal and fetal circulations in Rh(-) women. The mother's blood is drawn, and the test works by exploiting the resistance of HbF to acid, allowing fetal RBCs to be distinguished from maternal cells on a blood smear. Depending on the fraction of fetal RBCs present, this determines the dose of RhoGAM necessary. - Another 2CK Q gives ↑ fetal HR in 3rd trimester in woman who's in 2nd pregnancy who has (+) "anti-D titers." They ask reason why fetal HR is ↑ answer = "Rh isoimmunization" → destruction of fetal RBCs → ↓ oxygen delivery within fetal circulation → ↑ HR to compensate.
ABO type	<ul style="list-style-type: none"> - Most anti-A and -B Abs people have to opposing blood types are IgM, but people with O blood can have fractionally greater IgG; if mother with O blood has higher % of anti-A and -B Abs that are IgG, fetus can be symptomatic. - USMLE will give you O+ mom usually in first pregnancy and A or B fetus (can occur in Rh- women in second pregnancies, but the USMLE wants to assess you specifically know the ABO type of HDN, so they'll give O+ mom in first pregnancy).
Kell, Duffy, Kidd type	<ul style="list-style-type: none"> - Minor antigens beyond Rh (i.e., Kell, Duffy, Kidd) can sometimes cause HDN. - The process for isoimmunization is same as Rh. - What will happen is, an A+/B+/AB+ mother will have a second pregnancy where fetal hemolysis is occurring, but based on her blood type, you know it's not ABO or Rh type HDN. - The Q will say her blood titer for, e.g., Kell is high. The next best step is "check Kell status of the father." - In other words, since the mother has titers against Kell, you know she's Kell negative. So if the father's RBCs are Kell(+), the fetus is likely Kell(+), and that would explain the HDN.

Transfusion reactions	
Febrile non-hemolytic transfusion reaction (FNHTR)	<ul style="list-style-type: none"> - Caused by activation of donor WBCs when they come into contact with antibodies in the recipient's plasma. - This interaction triggers the release of cytokines from donor WBCs. - These cytokines then cause symptoms of fever and chills. - Coombs test is negative, since the process doesn't involve antibodies against donor RBCs. A (+) Coombs test means there are Abs against RBCs. - The vignette will be someone who gets a blood transfusion, and then within 2 hours gets fever + chills. They will then ask for the mechanism as the answer. I've seen them write it one of two ways: <ol style="list-style-type: none"> 1) Preformed antibodies against donor leukocyte antigens; and 2) Cytokine release from transfused blood. <ul style="list-style-type: none"> - Leukoreduction, a process that removes or reduces the number of WBCs from blood components before transfusion, can be used to mitigate risk of FNHTR by reducing probability of donor WBCs coming into contact with recipient antibodies.
Hemolytic (ABO mismatch)	<ul style="list-style-type: none"> - Caused by recipient antibodies against A and/or B antigens on donor RBCs.

	<ul style="list-style-type: none"> - This causes RBC agglutination and intravascular hemolysis, causing the release of hemoglobin into the bloodstream. - Binding of recipient antibodies to donor RBCs can also lead to complement activation and lysis of RBCs. - LDH can be increased in setting of hemolysis (RBCs are packed with LDH). - The vignette will be someone who gets fever, chills, and often flank pain within minutes of a blood transfusion. - Vignette can say, "10 minutes after the transfusion is started, the patient feels an 'impending sense of doom' and the transfusion is stopped" (sounds like MI, but NBME writes this). They then ask for next best step, which is antiglobulin test (another way of writing Coombs test).
Delayed transfusion reaction	<ul style="list-style-type: none"> - Caused by recipient antibodies against minor antigens on donor RBCs, such as Rh, Kell, Duffy, Kidd. - Coombs test is (+). - Vignette will be someone who had surgery + received RBCs intraoperatively + over the course of a week following the surgery, hemoglobin gradually decreases. The answer is then "Coombs (+); unconjugated bilirubin" as the combo that would be seen.
Transfusion-associated lung injury (TRALI)	<ul style="list-style-type: none"> - The answer on USMLE if a patient has an ARDS-like presentation with bilateral crackles and low O₂ sats <6 hours following a transfusion. - Mechanism is abnormal priming of neutrophils in the lung that react to cytokines within transfused blood products (this is straight from a CMS form). - Technically a type of non-cardiogenic pulmonary edema.
Transfusion-associated circulatory overload (TACO)	<ul style="list-style-type: none"> - Aka transfusion-induced hypervolemia. - Differs from TRALI in that this is a type of cardiogenic pulmonary edema (i.e., the left heart can't handle the ↑ hydrostatic pressure from ↑ volume, so transudation into the alveoli occurs). - The answer on USMLE if a patient has an ARDS-like presentation >6 hours following a transfusion, OR gets ARDS-like presentation following transfusion in the setting of cardiovascular disease. In other words, presents one of two ways: <p>1) They don't mention Hx of cardiovascular disease + the vignette will sound exactly like TRALI > 6 hours following a transfusion.</p> <ul style="list-style-type: none"> - 2CK form gives an elderly dude who received only 3 packs of RBCs + he develops bilateral crackles and low O₂ sats, but they say this occurs 12 hours after admission (not <6 hours as with TRALI), where the answer is "X-ray of the chest" as the next best step in diagnosis. The Q doesn't rely on you discerning TACO vs TRALI to get it right, but the explanation says it's TACO. <p>2) If a patient <i>with Hx of heart failure or MI</i> develops respiratory distress following transfusion of repeated blood products.</p> <ul style="list-style-type: none"> - A 2CK NBME Q gives a 72-yr-old with Hx of MI ten years ago who gets shortness of breath and bilateral crackles 30 minutes after transfusion with crystalloid solution and 4 packs of RBCs (they don't specify the volume of crystalloid in the Q). <p>In summary, if ARDS-like picture after transfusion:</p> <p>If <6 hours → TRALI. If >6 hours → TACO. If heart disease → TACO regardless of time frame.</p>

Heme/onc pharm points for IM	
Aspirin	<ul style="list-style-type: none"> - Irreversible cyclooxygenase (COX) 1&2 inhibitor. - Non-steroidal anti-inflammatory drug (NSAID). - Aka salicylic acid (salicylate). - Blocks synthesis of prostaglandins and platelet thromboxane A2. - ↓ prostaglandin means ↓ inflammation, pain, and body temperature. - ↓ thromboxane A2 means ↓ platelet clumping. - Many HY use cases on USMLE: <ul style="list-style-type: none"> - Atrial fibrillation (with low CHADS2 score – i.e., Congestive heart failure, Hypertension, Age >75, Diabetes, Stroke/TIA/Hx of emboli, with the S being worth 2 points). If 0 or 1 points, give aspirin to AF patient; if 2+ points, give warfarin. USMLE doesn't obsess over valvular vs non-valvular AF in terms of giving warfarin vs NOACs (e.g., dabigatran, apixaban); they will either give aspirin or warfarin as the answer choices. - Peripheral vascular disease and carotid stenosis → USMLE wants triad of anti-platelet therapy (aspirin alone sufficient on USMLE), statin, and ACEi or ARB. - Ischemic heart disease (i.e., patients who have angina pectoris) → nitrates are used for acute angina, but daily aspirin is also given to these patients. - Ischemic strokes after 4.5 hours has transpired; if <4.5 hours, give tPA. - Aspirin can cause GI bleeds (↓ prostaglandin → ↓ gastric mucosal barrier mucous production and protection), nephropathy (pre-renal, interstitial nephropathy, nephrogenic diabetes insipidus), asthma (inhibition of COX causes shunting of arachidonic acid down the lipoxygenase pathway → leukotriene synthesis → bronchoconstriction). - Never give aspirin to children due to Reye syndrome risk (defect in beta-oxidation, with cerebral edema and hepatitis). - Misoprostol is given to patients following PPIs if they have NSAID-induced gastric ulcers (misoprostol is PGE1 analogue). - Can cause high-anion gap mixed metabolic acidosis-respiratory alkalosis (S in MUDPILES).
Other NSAIDs	<ul style="list-style-type: none"> - "Other NSAIDs" = reversible COX inhibitors, in contrast to aspirin (irreversible). - Indomethacin → used for acute gout and pericarditis. - Ibuprofen → general NSAID used broadly for pain, fever, and autoimmune diseases (i.e., RA, IBD, SLE, etc.). - Naproxen → USMLE-favorite drug for causing GI bleeds and nephropathy; shows up on 2CK forms a lot. - Diclofenac, ketorolac (just know these names = NSAIDs). - 5-ASA compounds (mesalamine, sulfasalazine) used for IBD.
Acetaminophen	<ul style="list-style-type: none"> - Central-acting COX inhibitor. - Not considered an NSAID because it doesn't act peripherally. - Decreases pain and fever, but is not anti-inflammatory in the periphery. - First-line med for osteoarthritis (weight loss first Tx). NSAIDs not ideal first-line because they kill the kidneys + OA is non-inflammatory, so NSAIDs don't provide added benefit over acetaminophen. Patients with chronic pain who take NSAIDs frequently are at risk of nephropathy and GI bleeds. - Metabolite NAPQI causes massive hepatotoxicity. Activated charcoal can be given immediately after consumption, otherwise N-acetylcysteine HY as Tx. Latter regenerates reduced-glutathione, which neutralizes NAPQI.
Celecoxib	<ul style="list-style-type: none"> - Selective COX-2 inhibitor that does not cause GI bleeds. - Still can cause nephropathy. - NBME asks why celecoxib can increase the risk of MI → answer = decreases prostaglandin production without inhibiting platelets. - Can in theory be used for pain and inflammation.
Clopidogrel	<ul style="list-style-type: none"> - Anti-platelet agent; inhibits ADP P2Y12 receptor on platelets. MOA is HY.

	<ul style="list-style-type: none"> - Can be used to fulfill the anti-platelet component of the peripheral vascular disease and carotid stenosis triad (as mentioned before: 1) anti-platelet therapy; 2) statin; 3) ACEi or ARB). - In theory can be used for stenting procedures, but I haven't seen USMLE give a fuck. It's more that this use case is perpetuated in resources. - Can also be used in patients with ischemic heart disease who can't tolerate aspirin. - Prasugrel, ticlopidine, and ticagrelor drugs with same MOA, but not assessed.
Dipyridamole	<ul style="list-style-type: none"> - Phosphodiesterase-3 inhibitor; prevents breakdown of cAMP. - Causes arteriolar dilation + also an anti-platelet agent. USMLE really likes this – i.e., they will ask, “which of the following is both a vasodilator and anti-platelet agent?” → answer = dipyridamole or cilostazol (whichever is listed). - Dipyridamole/thallium is combo used frequently for pharmacologic stress testing. Arteriolar vasodilation causes HR to go up, where thallium uptake into myocardium can help visualize areas of ischemia.
Cilostazol	<ul style="list-style-type: none"> - Phosphodiesterase-3 inhibitor; prevents breakdown of cAMP. - Causes arteriolar dilation + also an anti-platelet agent, same as dipyridamole. - Used for intermittent claudication / peripheral vascular disease after a walking/exercise program is already prescribed. Do not choose cilostazol as a first treatment for peripheral vascular disease. Choose walking/exercise program first. Then, if they force you to choose a drug for additional management, choose cilostazol.
Abciximab	<ul style="list-style-type: none"> - GpIIb/IIIa inhibitor on platelets. - Prevents platelet aggregation (i.e., platelet-platelet interaction). - Don't confuse with GpIb, which is for platelet adhesion. vWF normally bridges GpIb on platelets to vascular endothelium / underlying collagen, and is unrelated. - Since physiologically, fibrinogen is normally what bridges GpIIb/IIIa on adjacent platelets, abciximab is considered to be a fibrinogen analogue. - Drugs such as tirofiban and eptifibatide have same MOA but aren't assessed.
tPA (alteplase), streptokinase	<ul style="list-style-type: none"> - Tissue plasminogen-activator activates plasminogen, which breaks down fibrin clots. - I've only seen this used twice on NBME forms: 1) for ischemic strokes within 4.5 hours; and 2) for pulmonary embolism where there is obstructive shock (i.e., PE with low BP).
Heparin	<ul style="list-style-type: none"> - Activates anti-thrombin III, leading to inactivation of thrombin (factor II) and factors IXa, Xa, XIa, and XIIa. - Used as a bridging agent to warfarin when patient needs anticoagulation. This is because warfarin, by inhibiting protein C as part of its function, temporarily makes the patient hypercoagulable. - Causes both an ↑ in PT and aPTT, but aPTT is used to monitor heparin over PT because aPTT is more accurate/sensitive to the effects of heparin. This is because heparin inhibits intrinsic pathway factors (i.e., IXa, Xa, and XIIa) <i>in addition to</i> the common pathway factors (i.e., thrombin and Xa). In other words, 5 clotting factors within the intrinsic pathway are affected by heparin, but only 2 within the extrinsic pathway are (i.e., the common pathway ones). - Subcutaneous enoxaparin (LMWH) used first-line for DVT and superficial thrombophlebitis. Heparin is also used for acute limb ischemia and vertebral artery dissection (clot can form within false lumen; asked on 2CK NBME). - USMLE won't ask about unfractionated heparin vs LMWH, but apparently unfractionated heparin is used in patients with 1) severe renal impairment and 2) in those who might need rapid-reversal due to uncertainty about dosing. In other words, unfractionated heparin can be reversed with protamine sulfate much faster than LMWH. - Heparin-induced thrombocytopenia (HIT) is exceedingly HY for USMLE. Mechanism is autoantibodies against heparin-platelet factor 4 (PF4) complex, where administration can lead to ↓ platelets. This is a type II hypersensitivity (platelets are cells). NBME can write the answer simply as “anti-platelet antibodies.” Treatment is cessation of heparin + give direct-thrombin inhibitor (e.g., dabigatran). Warfarin is wrong answer.

	A 2CK NBME Q simply has “direct-thrombin inhibitor” as the answer, without listing specific drug name.
Warfarin, dicoumarol	<ul style="list-style-type: none"> - Vitamin K epoxide reductase inhibitors, which prevent vitamin K from being recycled back to its active form. - Vitamin K normally is a cofactor for an enzyme called γ-glutamyl carboxylase, which activates clotting factors II (prothrombin), VII, IX, and X, as well as anti-clotting proteins C and S. - PT is used for monitoring over PTT because many of the intrinsic pathway clotting factors (PTT) are unaffected by warfarin, whereas most of the extrinsic pathway clotting factors (PT) are affected by warfarin. - International normalized ratio (INR) is the ratio of the patient’s PT to a control standard’s PT, where 2.0-3.0 is the usual target range for warfarin. - Highest yield use cases on USMLE are for maintenance anticoagulation therapy in patients who have DVT, prosthetic valves, or atrial fibrillation with elevated CHADS2 score. - As discussed earlier, heparin must be used as bridging agent initially with warfarin because warfarin’s inhibition of Protein C, which has a very short half-life, makes the drug initially pro-coagulable. - Warfarin levels are sensitive to drugs that inhibit or stimulate P-450. For example, P-450 inhibitors can \uparrow INR and cause bleeding diathesis; P-450 inducers can \downarrow INR and cause thromboses. - As discussed earlier, vitamin K deficiency due to broad-spectrum antibiotics causing depletion of bowel normal flora can \uparrow INR (i.e., \downarrow warfarin is required to inhibit clotting, but we haven’t changed dose). - Teratogenic; must be avoided in pregnancy. Warfarin is a small, lipophilic molecule that readily crosses the placenta. In contrast, heparin is a large, acidic polymer that does not cross the placenta. Warfarin can cause bleeding diathesis and bone abnormalities in the fetus. - Can cause skin necrosis in patients with protein C deficiency. - Slowly reversed with vitamin K (requires re-synthesis of clotting factors by the liver); quickly reversed by fresh frozen plasma (supplies clotting factors).
Dabigatran	<ul style="list-style-type: none"> - Direct-thrombin inhibitor. - Used for HIT. - Sometimes in patients with non-valvular AF with high CHADS2 score.
Apixaban	<ul style="list-style-type: none"> - Factor Xa inhibitor. Just know MOA. - USMLE doesn’t assess use cases, but can be given for non-valvular AF with high CHADS2 score.
Fondaparinux	<ul style="list-style-type: none"> - Factor Xa inhibitor. Just know MOA. - USMLE doesn’t assess use cases, but can be given for DVT and PE in place of heparin in some patients.
Irinotecan, topotecan	<ul style="list-style-type: none"> - Topoisomerase I inhibitors.
Etoposide, teniposide	<ul style="list-style-type: none"> - Eukaryotic topoisomerase II inhibitors; anti-cancer agents. - Don’t confuse with prokaryotic topoisomerase II (DNA gyrase) inhibitors, which refer to the fluoroquinolones (i.e., ciprofloxacin, levofloxacin).
Cisplatin	<ul style="list-style-type: none"> - Cross-linking agent. - Can cause nephro-, oto-, and neurotoxicity. - Chloride diuresis (i.e., normal saline) and amifostine can mitigate toxicity.
Doxorubicin (Adriamycin)	<ul style="list-style-type: none"> - Intercalating agent + produces free radicals. - Can cause dilated cardiomyopathy (HY). - Dexrazoxane mitigates toxicity by mopping up free radicals.
Bleomycin	<ul style="list-style-type: none"> - Induces DNA breaks. - Causes pulmonary fibrosis.
Carmustine, lomustine	<ul style="list-style-type: none"> - Alkylating agents.
Cyclophosphamide	<ul style="list-style-type: none"> - Guanine N7 alkylating agent.

	<ul style="list-style-type: none"> - Causes hemorrhagic cystitis (red urine). - Mesna mitigates toxicity by using a thiol (-SH) group to mop up acrolein, which is the toxic metabolite of cyclophosphamide that is toxic to uroepithelium.
5-fluorouracil	<ul style="list-style-type: none"> - Thymidylate synthase inhibitor. - Prevents conversion of dUMP to dTMP.
6-mercaptopurine	<ul style="list-style-type: none"> - Inhibits PRPP amidotransferase (enzyme in purine synthesis). - Requires xanthine oxidase for breakdown. - Allopurinol is a xanthine oxidase inhibitor that prevents tumor lysis syndrome in patients receiving chemotherapy for leukemia (lysis of leukemic cells releases nucleic acids into the blood, which are converted to uric acid). - Since 6-MP requires xanthine oxidase for breakdown, this means if patient is receiving 6-MP for chemotherapy, allopurinol cannot be given, otherwise 6-MP toxicity can result.
Azathioprine	<ul style="list-style-type: none"> - Pro-drug that is metabolized into 6-MP.
Mycophenolate mofetil	<ul style="list-style-type: none"> - Inhibits IMP dehydrogenase (an enzyme in purine synthesis). - Can be used for lupus nephritis.
Hydroxyurea	<ul style="list-style-type: none"> - Inhibits ribonucleotide reductase. - USMLE wants you to know it increases HbF in sickle cell to ↓ recurrence of painful crises. - Can be used to reduce bone marrow cell production in polycythemia vera to reduce hyperviscosity episodes. As discussed earlier, if USMLE gives you acute hyperviscosity syndrome, choose phlebotomy as best answer. Hydroxyurea is merely to decrease recurrence.
Microtubule drugs	<ul style="list-style-type: none"> - Vincristine, vinblastine, colchicine, griseofulvin, and -bendazoles (e.g., mebendazole) all inhibit microtubule polymerization. - Paclitaxel, docetaxel hyper-stabilize microtubules (i.e., prevent microtubule disassembly). - USMLE can ask for the protein these drugs interfere with → answer = tubulin. - Cells that are quickly dividing (i.e., GI mucosa, skin, hair follicles, bone marrow) are affected more than slowly dividing cells (e.g., myocardium). - If Q asks about the levels of which type of WBC are used to monitor for the toxic effects of chemotherapy, the answer is neutrophil (i.e., agranulocytosis). This is not limited to microtubule inhibitors, but I've seen USMLE ask this in relation to these drugs. - Vincristine is neurotoxic. - Colchicine is used for acute gout and pericarditis. - Griseofulvin is used orally for tinea capitis (patient only; don't give to close contacts; that distinction is asked on a 2CK form). - Mebendazole/albendazole are anti-helminthic agents, mostly for nematodes such as ascariasis, but can also be used for neurocysticercosis.
Imatinib	<ul style="list-style-type: none"> - Bcr/able tyrosine kinase inhibitor used to treat CML. - Can cause fluid retention / peripheral edema.
Erlotinib	<ul style="list-style-type: none"> - EGFR tyrosine kinase inhibitor used for non-small cell lung cancer.
Rituximab	<ul style="list-style-type: none"> - CD20 inhibitor on B cells. - Can ↑ risk of bacterial pneumonia (asked on NBME). This is because B cells mature into plasma cells, which make immunoglobulins, which are crucial for humoral immunity to fight bacterial infections.
Methotrexate	<ul style="list-style-type: none"> - Dihydrofolate reductase inhibitor (enzyme required in folate pathway). - First-line disease-modifying anti-rheumatic drug (DMARD) in rheumatoid arthritis. - First-line oral agent in plaque psoriasis that is non-responsive to topical agents, or for systemic psoriasis (arthritis). - Causes pulmonary fibrosis, mucositis (mouth ulcers due to neutropenia), and hepatotoxicity. - Toxicity mitigated with folinic acid (not folic acid), which is aka "leucovorin rescue."

IM Repro/Obgyn

Penile/testicular disorders	
Hypospadias	- Urethral meatus opens on underside of penis (ventral aspect).
Epispadias	- Urethral meatus opens on top of penis (dorsal aspect).
Phimosi	- Cannot retract the prepuce (foreskin). - In other words, cannot pull it back to expose the glans.
Paraphimosis	- Cannot reduce the prepuce. - In other words, once it is retracted, cannot replace it back over the glans. - Just remember that paraphimosis is the bad one / emergency.
Cryptorchidism	- Undescended testis. - Increased risk of infertility (\uparrow temperature within abdomen \rightarrow \downarrow spermatogenesis). - Increased risk of testicular carcinoma. - USMLE wants no treatment prior to age 6 months; after 6 months, perform orchidopexy.
Testicular torsion	- Acutely painful testis; medical emergency; can lead to ischemia and loss of testis. Can be caused by abnormality of the gubernaculum, which is a ligamentous cord that anchors the testis within the scrotum. This leads to "bell-clapper deformity," where improper anchoring = \uparrow risk of rotation. - Negative Prehn sign, which is failure of relief of pain upon lifting of the scrotum. Apparently this is an unreliable test in real life, but NBME vignettes can still mention it. In contrast, a (+) Prehn (relief of pain upon lifting the scrotum) is more indicative of epididymitis. - Negative cremasteric reflex, which is failure of the scrotal skin to retract upon palpation of the medial thigh. In contrast, a (+) cremasteric reflex (scrotal skin retracts) is more indicative of epididymitis. Normally, when the inner thigh is stroked, the cremaster muscle contracts and pulls up on the ipsilateral testis. In torsion, the twisted spermatic cord can impair the nerve fibers responsible for triggering the reflex. - USMLE wants Doppler ultrasonography as next best step, followed by surgery.
Epididymitis	- Inflammation/infection of epididymis. - (+) Prehn sign and (+) cremasteric reflex. - Chlamydia and gonorrhea are most common causes in males <35. - Over 35, <i>E. coli</i> is most likely. - The USMLE will not play games where they give you a borderline case and force you to guess. They will give you either a 25- or 45-year-old male. This also goes for prostatitis (same organisms). There is an NBME Q of a 45-year-old where the answer is <i>E. coli</i> , and chlamydia is wrong.
Torsion of appendix testis	- Not the same as torsion of testis. - Asked on a 2CK form. - Q will tell you there's a kid with a painful testis + the superior pole is blue + there's an intact cremasteric reflex ("regular torsion" it's not intact). - "Blue dot" sign = blue superior pole of testis. - Not my opinion if you think it's nitpicky or weird. Take it up with the NBME exam.
Peyronie disease	- Curvature deformity of penis caused by fibrous plaque within tunica albuginea. - Doesn't have to be treated unless causing functional impairment.
Orchitis	- Inflammation/infection of the testis. - Mumps is HY cause in unvaccinated / immigrants (sometimes implies unvaccinated). - If not caused by mumps virus, then the bacterial causes are same as epididymitis and prostatitis for young vs old (i.e., STIs vs <i>E. coli</i> , respectively).
Priapism	- Erection lasting longer than 4 hours. - Can be caused by sickle cell or by PDE-5 inhibitors (i.e., tadalafil/sildenafil). - Injection of alpha-1 agonist (i.e., phenylephrine) into the erectile tissue is treatment \rightarrow decreases blood flow due to blood vessel constriction.
Hydrocele	- Serous fluid collection within the scrotum between the layers of the tunica vaginalis surrounding the testis. - Mechanism is patent processes vaginalis.

	<ul style="list-style-type: none"> - The processus vaginalis is an embryonic outpouching of peritoneum that descends into the scrotum. It normally obliterates shortly after birth, but if it remains open, can cause hydrocele or indirect inguinal hernia. - Transilluminates when a light is shone to it. - USMLE wants no treatment before the age of 1; most spontaneously close.
Spermatocele	<ul style="list-style-type: none"> - Obscure serous fluid collection within the epididymis containing sperm. - Occurs usually in adult men (rather than neonates as with hydrocele). - Transilluminates similar to hydrocele. But once again, it's an older adult, not neonate.
Varicocele	<ul style="list-style-type: none"> - Dilation/congestion of pampiniform venous plexus draining the scrotum. - Does not transilluminate (in contrast to hydro- and spermatoceles). - Can be described as buzzy "bag of worms." Sounds too easy, but an NBME Q literally uses this colloquialism. - Can also be described as a heavy, dragging scrotum lower on the left. - Occurs almost always on the left side due to the anatomy of venous drainage of the testis. - On the left, we have left testicular vein → left renal vein → IVC. - On the right, we have right testicular vein → IVC ("right to IVC"). - The left testicular vein drains at a 90-degree angle into the left renal vein, creating a proclivity for hydrostatic pressure backup ipsilaterally. - There is a 2CK NBME Q where bilateral varicocele is the answer. Highly obscure, but just be aware it's somehow possible/exists. - Can occur due to left renal vein thrombosis in setting of nephrotic syndrome (loss of antithrombin III in the urine → hypercoagulable state).
Testicular cancer	<ul style="list-style-type: none"> - Seminoma most likely in teens and older. - Yolk sac tumor most likely in school-age kids and younger. - Hard nodule on testis is buzzy, but be aware of it as DDx for non-transilluminating testicular mass that does not present as classic hard nodule.

Ovarian neoplasms	
Serous cystadenoma	<ul style="list-style-type: none"> - Has Fallopian tube-like epithelium. - Can occur bilaterally. - Benign.
Serous cystadenocarcinoma	<ul style="list-style-type: none"> - Can have psammoma bodies. - 20-30% bilateral at time of diagnosis. - Malignant (i.e., has metastatic potential). I discuss tumor nomenclature in detail in the HY Path PDF.
Mucinous cystadenoma	<ul style="list-style-type: none"> - Has intestine-like epithelium. - Loculated or locular (meaning, has tiny cavities, like honeycomb). - Benign.
Mucinous cystadenocarcinoma	<ul style="list-style-type: none"> - Same as mucinous cystadenoma, but malignant. - Can cause pseudomyxoma peritonei, which is accumulation of mucin-producing tumor cells and gelatinous ascites in the peritoneal cavity.
Dysgerminoma	<ul style="list-style-type: none"> - Seminoma equivalent in females. - Large uniform cells with clear cytoplasm (same as seminoma). - Highly sensitive to chemo- and radiotherapy (same as seminoma). - Can occur idiopathically or in Turner syndrome. - LDH is a tumor marker.
Sertoli-Leydig cell tumor	<ul style="list-style-type: none"> - Produces androgens. - Can cause virilization in females.
Granulosa cell tumor	<ul style="list-style-type: none"> - Produces estrogen. - Can cause endometrial hyperplasia and ↑ risk of endometrial cancer due to unopposed estrogen. - NBME Q gives female with ovarian neoplasm + ↑ thickness of endometrial stripe + vaginal bleeding → answer for ovarian lesion = granulosa cell tumor.

Yolk sac tumor	<ul style="list-style-type: none"> - Aka endodermal sinus tumor. - The answer on USMLE for ovarian tumor in pediatrics (usually up to age 3). - Secretes AFP as tumor marker. - Schiller-Duval bodies on histo, which resemble glomeruli.
Embryonal carcinoma	<ul style="list-style-type: none"> - Aggressive and rapidly growing. - Undifferentiated/anaplastic cells on histo. - Secretes both AFP and hCG together as tumor markers. - Usually occurs in adult men, but can be seen as ovarian tumor also. The key for USMLE is that it's the answer if AFP and hCG are both high, whereas if only AFP is high, then the answer is yolk sac tumor. You can also remember yolk sac tumor is kids, whereas embryonal cancer is usually adults.
Brenner tumor	<ul style="list-style-type: none"> - Benign ovarian tumor that has urothelium (i.e., transitional cells). - Can appear tan/yellow.
Struma ovarii	<ul style="list-style-type: none"> - Benign ovarian tumor that secretes thyroid hormone.
Krukenberg tumor	<ul style="list-style-type: none"> - Gastric metastases to the ovaries bilaterally. - Has mucin-containing signet-ring cells on biopsy. - Spread to ovaries from stomach is usually hematogenous.

Endometrial cancer

- Highest yield point on USMLE is that it is caused by "unopposed estrogen," usually due to anovulation/PCOS.
- Estrogen normally stimulates growth of endometrium; progesterone prevents overgrowth.
- In anovulation/PCOS, no corpus luteum is formed, since the latter is the follicular remnant.
- The corpus luteum normally secretes progesterone to maintain the endometrial lining if fertilization occurs. If no corpus luteum is formed, there's no progesterone produced to balance estrogen. This leads to endometrial hyperplasia, which increases the risk of endometrial adenocarcinoma.
- USMLE can give an overweight female who's perimenopausal who has breakthrough bleeding (i.e., mid-cycle bleeding), or a post-menopausal woman with any vaginal bleeding, and they want endometrial biopsy as the answer. The fact that the patient has high BMI insinuates that anovulation/PCOS may have been a part of her past, where unopposed estrogen is a part of her history.
- Can occur secondarily as a result of granulosa cell tumor of the ovary (as discussed above). This is a rare cause of unopposed estrogen.
- Can occur in women who take hormone-replacement therapy (HRT) who stop taking the progesterone component (mentioned in one NBME Q).
- Can be associated with hereditary non-polyposis colorectal cancer (HNPCC; Lynch syndrome).

Fibroid points

- Fibroids are aka leiomyomata uteri and are most common benign tumor in women.
- They are smooth muscle tumors of the myometrium.
- Stain positive for desmin (muscle marker); can appear grossly as white tumors with whorled structure.
- Often found incidentally on ultrasound or autopsy.
- If fibroids are picked up incidentally on ultrasound, the answer is observe / follow-up. The highest yield point for USMLE is that these are not managed almost always.
- There is negligible risk of progression into leiomyosarcoma (malignant version that doesn't exist on USMLE). In other words, do not choose answers like myomectomy.
- If a woman has bleeding due to fibroids, OCPs and NSAIDs can be attempted in theory, although I have not seen USMLE assess these. Other treatments like leuprolide are also nonexistent on USMLE.

Vulvovaginal lesions	
Vulvovaginal carcinoma	<ul style="list-style-type: none"> - Cancer of the vagina and/or vulva. - Almost always squamous cell carcinoma due to HPV 16 or 18. - Can occur rarely due to lichen sclerosus.
Condylomata acuminata	<ul style="list-style-type: none"> - Aka warts; caused by HPV 6/11. - Present as painless, skin-colored or slightly hyperpigmented cauliflower-like popular lesions. - I discuss all of the STDs in more detail later.
Lichen sclerosus	<ul style="list-style-type: none"> - Presents as whitish-grey, rough, irritated or scratchy patch on the vulva or perineum. - Thought to be caused by a mix of chronic irritation and autoimmunity; not HPV-related. - Characterized by atrophy, hyperkeratosis, and a band of lymphocytes in the dermis. It is not neoplasia, dysplasia, or metaplasia. - USMLE wants biopsy as next best step to rule out SCC. If SCC is negative and the diagnosis is LS, USMLE wants topical steroid as treatment.
Sarcoma botryoides	<ul style="list-style-type: none"> - Rare as fuck. - Rhabdomyosarcoma of the vagina. - Seen in pediatrics as bunches of grapes protruding from the vagina.
Clear cell vaginal carcinoma	<ul style="list-style-type: none"> - Obscure cancer that occurs in women 30s-50s due to diethylstilbestrol (DES) exposure <i>in their mothers</i> while they were pregnant 30-50 years ago.
Bartholin gland cyst	<ul style="list-style-type: none"> - Shows up as a tender/painful bump at a 4- or 8-o'clock position on the vulva. - If the cyst becomes infected (i.e., warm and red), we call it Bartholin gland abscess. - USMLE wants "polymicrobial" as the most likely organism. - For cysts, sitz bath + warm compresses are first Tx. - For overt abscesses, drainage is the answer.
Vaginal foreign body	<ul style="list-style-type: none"> - Vignette will be a child with foul-smelling discharge from the vagina. - There will be no signs of physical trauma or lacerations (means not abuse).
Sexual abuse	<ul style="list-style-type: none"> - Can occur in children or elderly (I've seen both on NBME). - Vignette likes to mention lacerations. - There may or may not be discharge.

Cervical cancer + Pap smear screening
<ul style="list-style-type: none"> - Squamous cell carcinoma; occurs at the transitional zone between the stratified squamous ectocervix and columnar endocervix. - Caused by HPV 16/18. There are other strains students get pedantic about, but USMLE doesn't give a fuck. - Can cause vaginal bleeding + uni- or bilateral hydroureter / -nephrosis. - Pap smears should be started at age 21. If the vignette gives you a teenager who's sexually active, the answer is you test for STDs but do not do a Pap smear. - Perform Pap smear age 21-65. - From age 21-30, they are done every 3 years without HPV co-testing. - From age 30-65, the female has the option of continuing Paps every 3 years, or doing Pap-HPV co-testing every 5 years. - Pap smears are stopped at age 65. - If the female has a history of a high-grade squamous intra-epithelial lesion (HSIL) or cervical intra-epithelial neoplasia (CIN), Pap smears are continued after age 65. - Patients who have had hysterectomy due to cervical cancer should have continued Pap smears of the vaginal cuff. Patients with hysterectomy due to endometrial cancer do not. - Patients with HIV require two Pap smears in the first year following diagnosis (6 months apart), followed by annual Pap smears thereafter. The vignette will tell you HIV patient had normal Pap smear last year, and student is like, "Cool, she doesn't need one for another 2 years." No. This is important. You need to know HIV patients need once/year Paps.

- Low-grade squamous intra-epithelial lesions (LSIL) and atypical squamous cells of undetermined significance (ASC-US) are managed with either repeat Pap smear or HPV co-testing, where (+) vs (-) HPV test determines whether colposcopy + biopsy is performed. **USMLE will not** assess the algorithmic specifics. If you memorize the algorithm based on the female's age, you're wasting your time for USMLE purposes.
- HSIL on Pap smear is managed with immediate colposcopy + biopsy.
- CIN I is what we call LSIL that is confirmed on colposcopy + biopsy.
- CIN II/III is what we call HSIL that is confirmed on colposcopy + biopsy.
- CIN I has high rate of spontaneous regression. Repeat Paps are done in a year.
- CIN II/III requires excisional or ablational treatment due to higher risk of progression to invasive cervical cancer. Such treatments include LEEP, coning, cryotherapy, or laser ablation.
- Cone biopsy is also an answer on NBME for next best step in patient who has colposcopy performed for HSIL on Pap + "the entire squamocolumnar junction cannot be visualized." In other words, do a cone biopsy if colposcopy is insufficient.
- CIN III is **not** excised/ablated during pregnancy. HPV lesions (including warts) are known to get temporarily worse during pregnancy due to relative immunosuppression (biologic attempt to minimize attack against fetal antigens). In the post-partum period, CIN III lesions are evaluated for signs of regression over the course of weeks; if they do not regress, they are excised same as non-pregnant women with CIN II or III.

Cervical conditions confused with cancer

Cervical trauma	<ul style="list-style-type: none"> - Will present as vaginal bleeding in young woman usually within 12 hours of intercourse. - Doesn't sound hard/dramatic, but 2CK Qs can make vignettes somewhat nebulously where you second guess, i.e., they might say there's blood on the underwear. The key is that part of the Hx will mention post-coital bleeding.
Cervical polyp	<ul style="list-style-type: none"> - Benign, non-cancerous, pedunculated tumor that grows typically on the ectocervix. - Idiopathic. - Can cause metrorrhagia (mid-cycle bleeding). - Will not be described as ulcerated. If they say ulcerated, think cervical SCC.

Breast neoplasia + HY points

DCIS	<ul style="list-style-type: none"> - Most common malignant (i.e., has metastatic potential) breast cancer. - "Microcalcifications" on mammography = DCIS till proven otherwise. - 2CK wants "needle-guided open biopsy" as next best step; FNA is wrong. - Paget disease of breast (looks like a nipple with eczema in patient over 50) is often the cutaneous extension of an underlying DCIS.
Invasive ductal	<ul style="list-style-type: none"> - Invasive form of ductal carcinoma. - Cells on biopsy have stellate morphology.
LCIS	<ul style="list-style-type: none"> - Same as DCIS, malignant potential but not yet invaded. - Appears as linear rows of cells ("Indian file") on histo. This is supposedly due to ↓ E-cadherin expression, where the cells don't clump together the same way they do as with ductal carcinomas. I haven't seen USMLE give a fuck about this detail, but I'm mentioning it because if you ever talk to an attending about breast cancers, they become like hysterical over this detail.
Invasive lobular	<ul style="list-style-type: none"> - Invasive form of lobular carcinoma. - 20-30% bilateral.
Intraductal papilloma	<ul style="list-style-type: none"> - Unilateral bloody/rusty nipple discharge = intraductal papilloma till proven otherwise.
Inflammatory carcinoma	<ul style="list-style-type: none"> - Can appear as a red/inflamed breast, as though there's an infection. - Rubor (redness), dolor (pain), tumor (swelling), calor (heat). - Peau d'orange is an orange peel-appearing texture of the breast due to tethering of the skin by Coopers ligaments in the setting of blockage of lymphatic drainage by tumor cells.

Comedocarcinoma	<ul style="list-style-type: none"> - Cancer with cheese-like consistency. Nonexistent on USMLE. - Don't think I've ever seen it assessed.
Medullary carcinoma	<ul style="list-style-type: none"> - Another nonsense / garbage diagnosis on USMLE. - Mentioning comedo- and medullary carcinomas because if I don't, then at some point I'll get some whiny/mousy DMs from students about why I didn't mention them.
Fibroadenoma	<ul style="list-style-type: none"> - Most common breast tumor overall; benign. - Presents as rubbery, mobile, non-tender breast lump in woman 20s-30s. - Will appear as solid breast mass without calcification on ultrasound. - FNA is next best step to confirm Dx. If confirmed fibroadenoma, they do not need to be excised.
Cystosarcoma phyllodes	<ul style="list-style-type: none"> - Fast-growing breast lesion that appears "leaf-like" on light microscopy. - Can be benign or malignant based on histo.
BRCA points	<ul style="list-style-type: none"> - <i>BRCA1/2</i> are tumor suppressor genes but are inherited in an autosomal dominant fashion with incomplete penetrance (i.e., sometimes can skip a generation). A pedigree requiring you know this pattern is asked on NBME. - NBME also wants you to know that, with <i>BRCA</i> mutations, the molecular process that's fucked up is "recombinational double-stranded DNA repair."
Screening/Mx points	<ul style="list-style-type: none"> - For USMLE, mammography is done every two years between ages 50-74. - Since committees / cancer task forces have varying recommendations, the USMLE doesn't play trivia as far as "oh em gee do we start at 45 vs 50, etc." They won't be borderline about it. They will just give you a patient who's, e.g., 56 who needs a mammogram since she hasn't had one for two years. - If first degree family member (i.e., parent or sibling) has Hx of breast cancer, then start mammography at age 40, not 50. - Any breast screening done for a women under 30, do not do mammography on USMLE. Ultrasound is typically done. This is because younger women have denser breast tissue, making mammography less specific (i.e., more false-positives) and hence less reliable of a diagnostic modality. - Estrogen and progesterone receptor (ER/PR) positivity is correlated with better prognosis for breast cancers. This is partially because SERMs and aromatase inhibitors can be used as Tx. - HER2/neu positivity is correlated with worse prognosis. Trastuzumab (Herceptin) can be used to target HER2/neu. - Triple-negative ER/PR/HER2/neu is associated with bad prognosis due to ↑ aggressiveness, ↑ rates of recurrence, and ↑ risk of metastasis to lungs/brain. - 2CK NBME wants "bilateral mastectomy + oophorectomy" in patients who have confirmed <i>BRCA</i> mutation. - Breast cancer risk is ↑ as a result of HRT, even when progesterone is given as part of it. Breast cancer risk is ↑ as a result of ↑ absolute estrogen exposure the female has in her life. This has nothing to do with unopposed estrogen, which is the major risk factor for endometrial cancer. - Combined OCPs have been suggested in some literature as ↑ the risk of breast cancer, but there is no significance. They won't assess this on USMLE either way. But they do assess ↑ breast cancer risk as a result of HRT. - As I talked about before, the reason the only approved indication of HRT is severe vasomotor Sx (i.e., and not to maintain bone density, etc.) is because HRT ↑ the risk of breast cancer, thromboembolic events, MI, and stroke. This is because estrogen upregulates fibrinogen and factors V and VIII.

Other breast conditions	
Fibrocystic change	<ul style="list-style-type: none"> - Benign cystic alteration in breast tissue in women 20s-50s. - Shows up three ways on NBMEs: <ol style="list-style-type: none"> 1) Highly buzzy/classic presentation is a woman 20s-30s who has bilateral, waxing/waning breast tenderness over the course of her menstrual cycle; 2) Unilateral tenderness or sharp pain in one breast (students are often surprised that it's not always bilateral). 3) Painless, unilateral breast cyst in woman in her 40s that drains brown/greenish fluid → answer = fibrocystic change straight-up on the NBME. Call it weird all you want. Take it up with NBME, not me. - You do not need to biopsy or do ultrasound. It is a clinical diagnosis and Tx is symptomatic only (i.e., warm showers, evening primrose oil). - In theory, biopsy of fibrocystic change will show some buzzy findings: "sclerosing adenosis," apocrine metaplasia," and/or "blue dome cysts."
Simple breast cyst	<ul style="list-style-type: none"> - "Simple" means hypoechoic, or black on ultrasound. It reflects a fluid-filled cyst. - "Complex" means at least in some part hyperechoic, or white on ultrasound. It reflects a solid component to the cyst. - Simple cysts are observed and do not require FNA drainage unless they cause discomfort to the patient (e.g., large cysts). There is no specific size that requires drainage on USMLE. - There is an NBME Q where they say a woman was started on HRT three months ago and now has a simple cyst → answer = "biopsy of the lesion." So you should be aware that sudden growth in size can be indication for biopsy. - All complex cysts require FNA biopsy, similar to fibroadenoma.
Mastitis	<ul style="list-style-type: none"> - Classically presents as red, cracked, fissured nipple in breastfeeding woman. - Usually caused by <i>S. aureus</i>, but Group A Strep also possible. - USMLE wants oral dicloxacillin (not doxycycline) + continue breastfeeding through the affected breast as treatment. There is no risk of harm to the neonate. Methicillin-class beta-lactams (e.g., dicloxacillin) and first-generation cephalosporins (e.g., cephalexin) are equivalent on USMLE for all intents and purposes. They both treat <i>S. aureus</i> skin infections. - High-yield point is that mastitis need not affect the nipple and can present as a red, warm, tender, non-fluctuant mass of the breast. When we talk about infection of the breast, non-fluctuant = mastitis; fluctuant = abscess. This is asked insidiously on a 2CK form and students get it wrong all the time thinking it's abscess – i.e., "They say it's a warm, red, tender mass of the breast though!" Yeah, but they say non-fluctuant, not fluctuant. Not my issue if you get emotional over dumb shit.
Abscess	<ul style="list-style-type: none"> - Warm, red, tender <i>fluctuant</i> mass of the breast. - Drain as next best step.
Galactocele	<ul style="list-style-type: none"> - Aka milk retention cyst; usually seen in recently breastfeeding women. - Often confused with breast abscess. - Can present as painless or tender fluctuant mass of the breast that is peri-areolar. - USMLE will say the patient is afebrile and that the lesion is not warm or red. - Tx is warm compresses followed by drainage.
Ductal ectasia	<ul style="list-style-type: none"> - As the name implies, this is dilation of lactiferous ducts. - Diagnosis of exclusion on USMLE (i.e., we eliminate to get there). - Presents 2/3 Qs as an inverted nipple. - Presents 1/3 Qs as some random breast lesion where they say biopsy shows "dilation of the ducts," which is what the name means.
Virginal breast hypertrophy	<ul style="list-style-type: none"> - Virginal breast hypertrophy is benign asymmetric growth of the breasts that can occur in young women. USMLE will try to trick you into thinking it's sinister by saying a first-degree relative had breast cancer. - They will say 16-year-old girl has large breast lump under the nipple on one side. Answer is just follow-up / observe.
Gynecomastia	<ul style="list-style-type: none"> - Physiologic gynecomastia can occur in teenage boys on USMLE, where there can be ↑ breast tissue, either tender or not, occurring uni- or bilaterally. Just observe.

	<ul style="list-style-type: none"> - Can occur as a result of ↑ estrogen in liver failure, or due to certain drugs like cimetidine, spironolactone, ketoconazole, or even marijuana. - Caused by direct estrogen effect on breast. It is not caused by prolactin. - As I talked about earlier, an NBME Q gives gynecomastia in a male patient taking hCG. They ask for the mechanism → answer = “testis producing estrogen.” They can also have as answer “estrogen; direct effect on breast.” The reason this makes sense is because, since hCG shares the same alpha-subunit with LH and FSH (and TSH), giving hCG is as though we are giving LH and FSH at the same time. So LH effect → androgen production; FSH effect → aromatase production → therefore androgens are converted to estrogens in the testis → mechanism via which we could get gynecomastia.
Necrosis	<ul style="list-style-type: none"> - Non-enzymatic fat necrosis of breast due to trauma; can calcify. - Don't confuse with enzymatic fat necrosis, which is acute pancreatitis. - Can occur due to overt trauma (e.g., getting hit by softball) or sometimes by tight-fitting sports bras.


Other ovarian conditions	
Ruptured ovarian cyst	<ul style="list-style-type: none"> - Presents as sudden, sharp pain in an adnexa (adnexa = combo of Fallopian tube + ovary). - The Q will often say there is 10-15 mL of serosanguineous fluid in pouch of Douglas on culdocentesis (means aspiration of pouch of Douglas). - The Q will say there is no mass / will not mention mass. - Treated symptomatically (i.e., NSAID). Do not do laparoscopy.
Adnexal/ovarian torsion	<ul style="list-style-type: none"> - 3/4 Qs will give intermittent adnexal pain that becomes constant over hours to weeks (I've seen NBME give both time frames). - 1/4 Qs will just say few-hour Hx of constant pain without the intermittent detail first. - Presents as “large” adnexal mass (i.e., 8 x 12-cm). - There will be no mention of fluid in pouch of Douglas. - Treatment is laparoscopic detorsion. - Tricky detail is that the biggest risk factor is a pre-existing anatomic abnormality (e.g., cyst). So if they say Hx of cyst + now has large adnexal mass and pain, that is torsion, not ruptured cyst.
Theca-lutein cyst	<ul style="list-style-type: none"> - Arises from theca cells of the ovary; usually bilateral. - Frequently associated with conditions where hCG is very high, such as moles, multiple gestation pregnancies, or fertility drug use. - Can occasionally bleed, where the answer is “hemorrhagic theca-lutein cyst” as a diagnosis of exclusion (i.e., we eliminate to get there), where endometrioid cyst can be eliminated because the Q won't mention anything about dysmenorrhea or signs of endometriosis.
Endometrioid cyst	<ul style="list-style-type: none"> - Aka endometrioma, or “chocolate cyst.” - Cyst filled with endometrial tissue that bleeds. - Occurs in endometriosis (endometrial tissue growing outside the myometrium, usually on the ovary, as with this case; discussed more later).
Dermoid cyst	<ul style="list-style-type: none"> - Aka mature cystic teratoma. - Contains tissue from multiple germ layers – i.e., hair, skin, teeth, etc. - Can calcify.

Testicular cancer	
Seminoma	<ul style="list-style-type: none"> - Most common testicular cancer; occurs teenage years and older. - Large, uniform cells with watery cytoplasm. - Chemo- and radiosensitive. - Placental ALP can be a tumor marker.
Yolk sac tumor	<ul style="list-style-type: none"> - Aka endodermal sinus tumor. - Most common in kids under 3. - AFP is tumor marker.
Embryonal carcinoma	<ul style="list-style-type: none"> - Immature/anaplastic cells. - Combined AFP and hCG are tumor markers. - Usually adult men.
Sertoli-Leydig cell tumor	<ul style="list-style-type: none"> - Secrete androgens. - Can cause gynecomastia (shows up on NBME). This is because ↑ androgens can be aromatized into estrogens.
Granulosa cell tumor	<ul style="list-style-type: none"> - Secretes estrogen. - Can also cause gynecomastia. If NBME gives you Q with Sertoli-Leydig cell tumor causing gynecomastia, they won't simultaneously list granulosa cell tumor as an answer.
Choriocarcinoma	<ul style="list-style-type: none"> - Composed of syncytiotrophoblastic placental cells. - Can occur in males, yes. Usually 20s-30s. - ↑↑ hCG as tumor marker.

Prostate cancer vs BPH points	
Prostate cancer	<ul style="list-style-type: none"> - Adenocarcinoma (i.e., glandular); most common cancer in men. - Stimulated by DHT. - Causes osteoblastic metastases (highest yield point on USMLE). - Can present as random guy over 50 with no PMHx who just suddenly has neurologic symptoms in the legs and two blastic lesions in his spine picked up on MRI. - If neuro Sx are present due to spinal mets, give IV methylprednisolone. - If no neuro Sx are present and they just say vertebral blastic lesions, answer will be radiotherapy. I've seen distractor answers in this case such as "morphine + corticosteroids," where the student says, "I thought we give steroids though." Yeah, if the patient has neuro Sx, which he doesn't here, plus jumping to morphine before trying other pain management first is wrong. - Orchiectomy will ↓ androgen production → leads to atrophy and shrinkage of prostatic cancer cells. - Flutamide blocks androgen receptor. It is given prior to leuprolide, which is a GnRH receptor agonist that, when given continuously, causes desensitization at GnRH receptor. Since leuprolide can ↑ LH and FSH prior to desensitization, the flutamide is given first. - Prostate-specific antigen (PSA) will often be elevated. Free-PSA (i.e., not bound to protein) is low compared to bound-PSA in prostate cancer. - Gleason scoring is used to grade prostate cancer. - The parasympathetic nerves (for erection) are at greatest risk of injury during radical prostatectomy (asked somewhere on NBMEs).
BPH	<ul style="list-style-type: none"> - Benign prostatic hyperplasia. - All old dudes have enlarged prostates due to lifetime exposure to DHT, which causes prostatic enlargement. - Presents as dribbling, hesitancy commencing urination, or interrupted stream in a male over 60 (but usually 70s+). - "Old dude + high creatinine = BPH till proven otherwise." - Discontinue anti-cholinergic meds because they cause urinary retention. This concept shows up a lot on NBMEs. Three classes of drugs in particular:

	<p>1) First-gen H1 blockers (i.e., diphenhydramine, chlorpheniramine);</p> <p>2) TCAs (i.e., amitriptyline).</p> <p>3) Anti-psychotics.</p> <p>- You'll get a Q where an older male has high Cr and then the answer is just "discontinue anticholinergic meds," or "discontinue the diphenhydramine."</p> <p>- Can be described as "nodular" on palpation.</p> <p>- Prostate-specific antigen (PSA) will often be elevated. Free-PSA is high compared to bound-PSA in BPH.</p> <p>- Tx is alpha-1 blocker, such as tamsulosin/terazosin; or the 5-alpha-reductase inhibitor, finasteride.</p> <p>- Transurethral resection of prostate (TURP) for refractory cases.</p>
--	---

HY STDs	
Human papilloma virus	<p>- HPV 6/11 cause condylomata acuminata (warts). This is not limited to the genitalia and can cause laryngeal papillomatosis in neonates (warts of the vocal cords), which is asked on NBME.</p> <p>- HPV 16/18 cause squamous cell carcinoma of genitalia/anus; risk of overt SCC is ↑ in immunocompromised (i.e., HIV in MSM) and heavy smoking.</p>
<i>Chlamydia trachomatis</i>	<p>- The "regular" STD are <i>Chlamydia</i> D-K strains.</p> <p>- Causes mucopurulent discharge.</p> <p>- Can advance to pelvic inflammatory disease (PID) in females, which is when infection causes inflammation and scarring of Fallopian tubes, leading to ↑ risk of ectopic pregnancy.</p> <p>- Obligate intracellular, so cannot be grown. Discharge will show WBCs under light microscopy with no organisms. If the vignette tells you no organisms grow, this is pass-level for <i>Chlamydia</i>.</p> <p>- Treat with stat/one-off oral dose of azithromycin; can cause GI disturbance.</p> <p>- Can also be treated with one-week of BID (i.e., twice/day) doxycycline; cannot be taken with dairy or divalent cations (impaired absorption); can also cause photosensitivity; considered to be slightly more efficacious than azithromycin but much more annoying and arduous to take.</p> <p>- USMLE won't play trivia as to which drug is first-line; there will only be one correct answer. For example, doxy is not given in pregnancy, so if you're forced to choose between the two, in this case you know it's azithromycin (or even sometimes erythromycin in pregnancy).</p> <p>- Doxy isn't given in pregnancy because it can cause teeth discoloration in the eventual neonate.</p> <p>- <i>Chlamydia</i> can cause reactive arthritis (triad of urethritis, arthritis, and eye-itis – i.e., any inflammation of the eye, e.g., conjunctivitis, anterior uveitis, etc.).</p> <p>- To prevent ophthalmia neonatorum (neonatal conjunctivitis), treat the female while she is pregnant; to Tx the actual condition in neonates, give oral erythromycin. Conjunctivitis in a neonate can lead to <i>Chlamydia</i> pneumonia.</p> <p>- <i>Chlamydia</i> A-C are not STDs and cause trachoma (cause of blindness in Africa).</p> <p>- <i>Chlamydia</i> L1-3 cause lymphogranuloma venereum (anal strictures).</p>
<i>Neisseria gonorrhea</i>	<p>- Causes mucopurulent discharge, same as <i>Chlamydia</i>.</p> <p>- Gram-negative diplococci on light microscopy.</p> <p>- Same as with <i>Chlamydia</i>, can advance to PID, with ↑ risk of ectopic pregnancy.</p> <p>- Doesn't cause reactive arthritis; it causes gonococcal arthritis, which will present one of two ways on NBME: 1) monoarthritis of the knee; or 2) triad of mono- or polyarthritis + cutaneous papules/pustules + tenosynovitis (inflammation of tendon sheaths; stems like to give deQuervain tenosynovitis).</p> <p>- Treatment is IM ceftriaxone.</p> <p>- Always cotreat for <i>Chlamydia</i>. In other words, if the gram-(-) diplococci are seen under LM, there's no way to know if <i>Chlamydia</i> is also there or not since the</p>

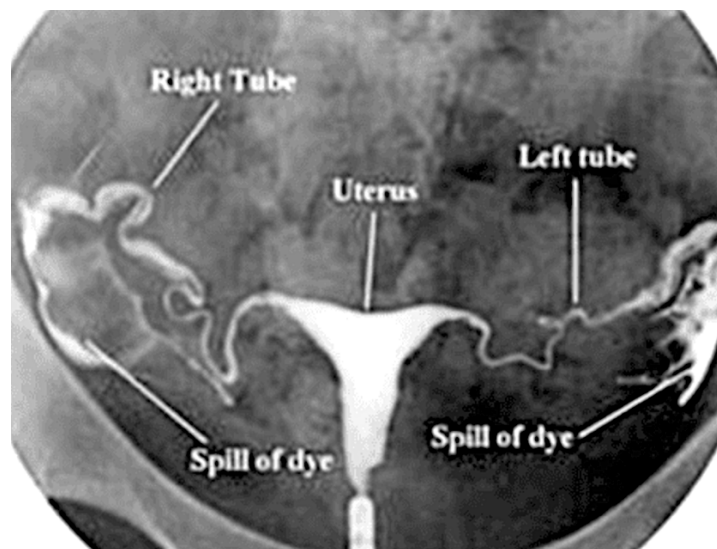
	<p>latter shows no organisms, so if a patient has <i>Gonorrhea</i>, the proper Tx is IM ceftriaxone, PLUS either oral azithromycin or doxycycline.</p> <ul style="list-style-type: none"> - If patient develops PID despite having been treated early with ceftriaxone for <i>Gonorrhea</i>, the answer for why this happened can be "Hx of improper antibiotic treatment," where the patient was supposed to be cotreated for <i>Chlamydia</i> with azithromycin but was only given the ceftriaxone for <i>Gonorrhea</i>. - If patient presents with PID who's septic (i.e., high fever, tachy, high WBCs), USMLE wants "admit to hospital + IV antibiotics," not the outpatient combo of IM + oral. - 2CK form assesses that if an asymptomatic patient comes in after a partner tested positive for <i>Gonorrhea</i> or <i>Chlamydia</i>, the answer is give treatment without waiting for test results. - Erythromycin ointment is used on neonates as prophylaxis for conjunctivitis; if neonate already has it, give IM cefotaxime (preferred 3rd-gen cephalosporin in peds if listed).
<i>Trichomonas vaginalis</i>	<ul style="list-style-type: none"> - Causes trichomoniasis. - Flagellated protozoan seen on wet mount. - Presents as yellow-green discharge. - Can cause "strawberry cervix," or punctate hemorrhages on the cervix. If they don't say this, they can sometimes say yellow-green discharge + a vaginal canal that is erythematous. - Treat with metronidazole for patient and partner (high rate of reinfection).
<i>Gardnerella vaginalis</i>	<ul style="list-style-type: none"> - Causes bacterial vaginosis. - Gram-negative rod that causes a thin grey/watery discharge. - Positive whiff test (KOH prep causes fish-like odor). - Clue cells exceedingly HY (squamous epithelial cells studded with bacteria). They want you to know this image for USMLE: 
<i>Candida spp.</i>	<ul style="list-style-type: none"> - Causes candidiasis. - Buzzy thick, white, cottage cheese-like discharge in ~2/3 of questions. - The other ~1/3 of Qs will mention an itchy/erythematous vaginal canal without any overt discharge (in contrast to trichomoniasis which can present with erythema of the vagina but has characteristic yellow-green discharge). - Treat with topical nystatin or oral fluconazole.
<i>Treponema pallidum</i>	<ul style="list-style-type: none"> - Causes Syphilis. - Spirochete (spiral-shaped bacterium) visible under dark-field microscopy. - Primary syphilis = painless chancre (painless ulcer) on genitalia. - Secondary syphilis = 6 weeks to 6 months after appearance and disappearance of the initial chancre, patient can get body rash that includes palms + soles, and condylomata lata (painless genital plaques).

	<ul style="list-style-type: none"> - Tertiary syphilis = years later, patient can get gummas (appear as painless chancres but are on other areas of the body such as the face/nose), arthritis, and ascending aortitis (tree-barking of vasa vasorum). - Neurosyphilis can occur at any stage; it is not sequential where we have 1 → 2 → 3 → neurosyphilis. There is a 2CK Neuro Q that gives neurosyphilis in an 18-year-old. - Neurosyphilis presents as tabes dorsalis (obliteration of dorsal columns, with loss of vibration/proprioception + a positive Romberg sign, where patient falls over when standing with eyes closed), Argyll-Robertson pupil (i.e., “prostitute pupil”; accommodates but doesn’t react), and “stroke without hypertension” (i.e., sometimes findings akin to stroke but in a younger patient). - Diagnosis of primary syphilis is made via visualizing the spirochetes from a chancre scraping under dark-field microscopy. - Diagnosis of secondary, tertiary, and neurosyphilis can be done with serology, where a VDRL and/or RPR is done first (sensitive but not specific); an FTA is done as confirmatory (specific but not sensitive). - VDRL test mixes the patient's serum with cardiolipin antigen. If antibodies against <i>T. pallidum</i> are present, the test demonstrates clumping/flocculation. The RPR enhances this reaction by using charcoal particles. There is an NBME Q floating around where they say something about a patient whose test results demonstrate clumping with charcoal particles, and the answer is SLE. - Patients with SLE who have anti-phospholipid syndrome can get false-positive VDRL tests because this syndrome is often caused by antibodies against cardiolipin (in SLE, we simply call these antibodies “lupus anticoagulant”). - FTA mixes a patient's serum with fluorescent <i>Treponema</i> antibodies. If binding occurs, this confirms the diagnosis of syphilis. - USMLE will show you 24-year-old male with rash on his back + KOH prep is negative + ask what’s most likely to diagnose → answer = FTA. - Treatment for all syphilis types is penicillin. - If patient has Hx of anaphylaxis to beta-lactams but is pregnant or has tertiary or neurosyphilis, the answer is desensitize + give penicillin. This is because penicillin is the most efficacious and needs to be given in severe cases. - If patient has Hx of mere rash to beta-lactams, but not anaphylaxis, then the beta-lactam can be given anyway.
HSV 1/2	<ul style="list-style-type: none"> - Herpes simplex virus 1/2. - Causes painful vesicular lesions that recur at varying intervals (usually months). - Primary infection is most severe, often with fever, regional lymphadenopathy, burning/stinging/itching pain (herpetic neuralgia), and many vesicles. - Recurrences are often less severe and preceded by herpetic neuralgia. - HSV1/2 can also cause encephalitis (confusion + blood in CSF due to temporal lobe hemorrhage) and herpetic whitlow (vesicle[s] on the finger). - Viral culture can be negative in stem (not 100% sensitive). - Treat with acyclovir (or valacyclovir).
<i>Haemophilus ducreyi</i>	<ul style="list-style-type: none"> - Causes chancroid, which is a painful ulcer. - Gram-negative rod. - “-Oid” means looks like but ain’t. So it looks like a syphilitic chancre, but it’s not. - The syphilitic chancre is painless; the <i>H. ducreyi</i> lesion is painful. - Often a wrong/distractor answer for HSV Qs, where students get trigger-happy and erroneously choose the weird answer (<i>H. ducreyi</i>). - Chancroid will be the answer if they tell you there’s a single painful genital lesion in someone who went abroad, classically backpacking in Africa or South America. - If they tell you there’s a single, small painful lesion, <i>but that it’s a recurrence</i>, this is HSV, not <i>H. ducreyi</i>. The latter is bacterial and doesn’t cause recurrences the way HSV does; HSV can rarely appear as a single vesicle. - There is a 2CK NBME Q where answer is actually <i>H. ducreyi</i>, but I once again caution that this is usually a wrong answer, so be careful. But I have seen it correct as a one-off.

	- USMLE won't assess treatment, but either azithromycin or ceftriaxone is considered first-line.
--	--

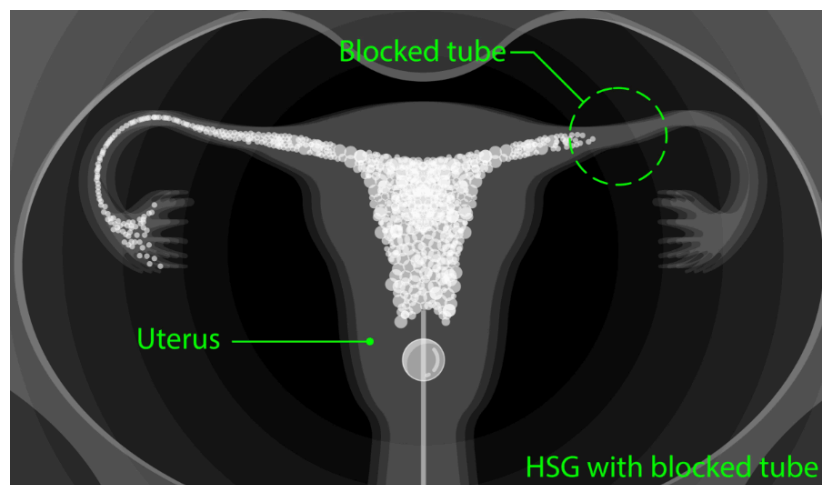
Pelvic inflammatory disease (PID)

- As discussed earlier, is caused by either *Chlamydia* or *Gonorrhea*.
- When the infection ascends the uterus and Fallopian tubes, it can lead to inflammation and scarring, thereby increasing the risk for ectopic pregnancy (i.e., loss of Fallopian tube cilia leads to premature implantation usually in the ampulla of the Fallopian tube).
- Adnexal and **cervical motion tenderness** are buzzy. But particularly the latter. If they say cervical motion tenderness, you know right away they're talking about PID.
- USMLE wants you to know that the Fallopian tubes are normally open on both ends, where the release of the ovum from the ruptured Graafian follicle is "caught" by the fimbriae of the Fallopian tube, prior to its transit to the uterus. Because the Fallopian tubes are open on both ends, when a hysterosalpingogram is performed, spillage of dye bilaterally into the peritoneal cavity *is normal*.



Normal hysterosalpingogram

- If there is Hx of PID and the Fallopian tube is scarred, it may be sealed, where the hysterosalpingogram shows failure of spillage.



- If the Q tells you a girl has PID and is treated with antibiotics but has persistent fever and adnexal pain, next best step = ultrasound to look for **tubo-ovarian abscess**, which is a potential sequela of PID.

- Extension of PID to the liver capsule is called Fitz-Hugh-Curtis syndrome.

TORCHes infections	
- Refers to congenital infections in the neonate due to infection in the mother while pregnant.	
Toxoplasmosis	<ul style="list-style-type: none"> - Presents as HY triad in neonate of 1) hydrocephalus, 2) chorioretinitis, and 3) intracranial calcifications. - They don't have to say the mom sat in a litter box with her cat during pregnancy. - Can be acquired from pork consumption.
Other (Parvovirus B19, VZV)	<ul style="list-style-type: none"> - Parvo B19 can cause aplastic anemia <i>in utero</i> or in the neonate, with increased risk in sickle cell. - Aplastic anemia = all 3 hematologic cell lines are down (i.e., RBCs, WBCs, and platelets). - Can sometimes cause a pure-RBC aplasia (i.e., only RBCs down). - The term "fetal hydrops" refers to heart failure <i>in utero</i>, and can suggest severe anemia, such as with maternal Parvo infection. In other words, the stem can say the mom had a flu-like illness or cold, followed by hydrops in the fetus → answer = Parvo. - Q can ask how to confirm Parvo infection in neonate if suspected → answer = check Parvo IgM titers in neonate. - Varicella (VZV) during pregnancy can cause microcephaly and limb hypoplasia. - If mother contracts VZV for the first time between 5 days prior to parturition until 2 days after, Varicella immunoglobulin must be given to the neonate. - Kids with congenital VZV syndrome (as well as those who are immunocompromised), are at increased risk of pediatric shingles (just know this Dx exists / "is a thing"). - If neonate is exposed to child with active varicella, if the mother of the neonate previously had chickenpox or was vaccinated, you do not need to give VZV IVIG to the neonate. This is because the neonate has passive immunity from the transplacental IgG. - Should be noted that pregnant women who contract VZV can get pneumonia from it (sounds weird, but it's a factoid you could be aware of).
Rubella	<ul style="list-style-type: none"> - Presents as patent ductus arteriosus (PDA) in a neonate. Exceedingly HY / pass-level. - Cataracts and deafness also possible. - Q doesn't need to say mom had rash while pregnant. Sometimes pregnant women get only arthritis. This is not unique to rubella, but I'm just mentioning it because the stem can say she had arthritis but no rash, and student is like "Well it couldn't have been rubella in the mom then." No. Adults sometimes get only arthritis if they contract rubella or measles. - MMR vaccine is live-attenuated and is contraindicated during pregnancy due to theoretical risk to the fetus. If a woman inadvertently receives the vaccine while pregnant or within the month prior to pregnancy, it is not an indication for abortion, but risks to the fetus are increased and proper monitoring is important.
CMV	<ul style="list-style-type: none"> - Congenital cytomegalovirus is a diagnosis of exclusion on NBME Qs, as per my observation (i.e., we eliminate to get there). - Congenital deafness, hepatomegaly, "blueberry muffin rash," and intracranial calcifications are HY, but these are non-specific and seen in other conditions too. - The USMLE Q might say, "Kid is born with intracranial calcifications, hepatomegaly, and deafness." And the student says, "Aren't calcifications toxo?" Yes, but toxo is the strict triad as mentioned above. The student might also say, "Well can't deafness be rubella or syphilis." Yes, but for rubella they always mention PDA, and for syphilis they always mention unique findings like tooth or shin abnormalities (discussed below). So we eliminate to get there and are left with CMV. It's a bit circuitous, but it's what I've observed they do with CMV Qs. - CMV causes owl-eye appearance of cells due to intranuclear inclusions. - Tx = ganciclovir. MOA is DNA polymerase inhibitor. Mechanism of resistance is alterations to viral thymidine kinase.
Herpes/HIV	<ul style="list-style-type: none"> - Vaginal HSV1/2 infection in mother can lead to vertical transmission, increasing risk for encephalitis in neonate.

	<ul style="list-style-type: none"> - If a pregnant woman experiences prodromal symptoms (i.e., tingling, burning, etc.), even if no visible lesions are present, C-section is still recommended. - If a pregnant woman has predictable intervals of vesicular episodes, acyclovir is often given within 4-6 weeks of parturition to decrease risk of peripartum episode. - HIV in pregnancy is HY. Most important point is that highly active anti-retroviral therapy (HAART) is started immediately in any HIV patient regardless of CD4 count and that it is three-drug therapy. - Efavirenz (an NNRTI) is avoided in pregnancy. - TMP/SMX is avoided in first-trimester, or if woman is immediately trying to conceive, even if CD4 count is under 200. It is okay to use in 2nd and 3rd trimesters. - Intrapartum zidovudine is given to HIV (+) mothers + C-section is performed. - Zidovudine is given to the neonate within 6-12 hours of birth + given for 6 weeks. - HIV is present in breastmilk. It is generally recommended to avoid breastfeeding if mother is HIV (+). If the mother's viral load is undetectable and she is on continued HAART, transmission to neonate might not occur, but it is still advised against.
Syphilis	<ul style="list-style-type: none"> - Highest yield point is that it can cause tooth abnormalities (mulberry molars/incisors). - Can cause "saber shins" (bone abnormalities), saddle nose, deafness, and cataracts.

Pubertal development						
Tanner stage	Male genital appearance	Male genital description	Female pubic hair appearance	Pubic hair description	Breast appearance	Breast description
1		Testicular volume <3ml		No pubic hair		Elevation of papilla only
2		Testicular volume <3ml, change in texture to scrotal skin		Sparse growth chiefly along the labia/base of penis		Breast bud stage
3		Increase in size of penis with further testicular enlargement		Darker, coarser, more curled hair		Enlargement of breast and areola
4		Further enlargement of penis and testicles with development of glans penis		Adult type hair over a smaller area		Projection of the areola and papilla
5		Adult size and shape		Spread to the medial surface of the thighs		Recession of the areola to the contour of the breast, projection of papilla only

- USMLE wants you to know that at Tanner stage 3, "menarche is imminent." That is an answer straight-up on one of the 2CK forms, but there are also various Repro Qs where mom will bring in her daughter who's 13/14, who's never had a menstrual period, and they'll say she's either Tanner stage 2 or 3, and the answer is just "schedule follow-up in 6 months."

- Turner syndrome can present with Tanner stage 1-2 breasts and 4-5 pubic/axillary hair. The latter are due to the effects of adrenal, rather than ovarian, androgens. In other words, don't be confused if you get a Turner syndrome Q and they say Tanner stage 4 pubic hair.

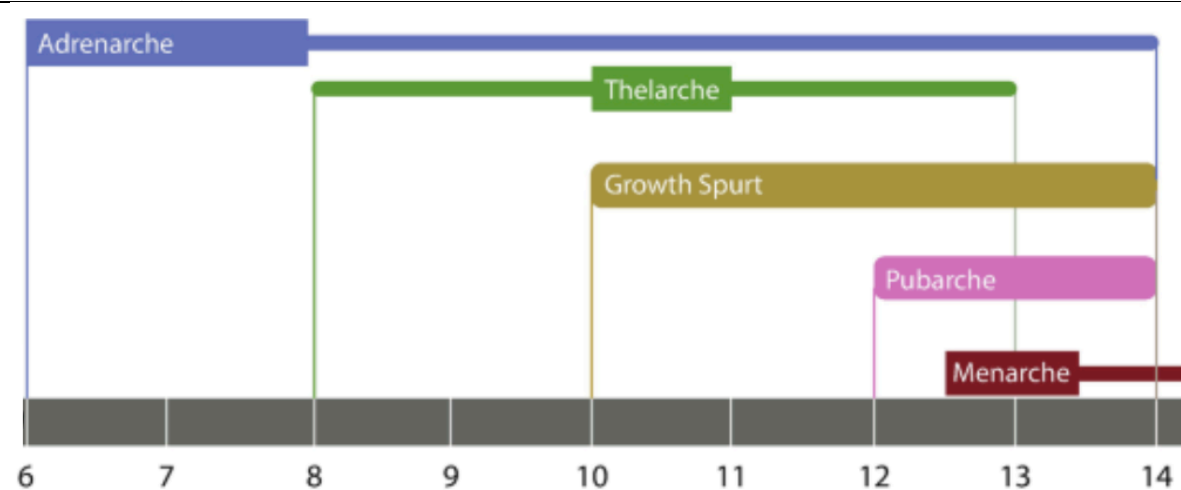
- In androgen insensitivity syndrome (46XY karyotype, but female phenotype), breast development is normal (i.e., Tanner 4-5), but pubic/axillary hair are Tanner stage 1 (i.e., scant/absent).

- Bone age refers to degree of maturation of a child's bones via radiographic examination.

- USMLE wants you to know that bone age < chronologic age means the short child will catch up (i.e., the growth chart is merely right-shifted). This is called constitutional short stature. The vignette will usually say both parents are average height. For example, a 14-yr-old boy is shortest in his class but has a bone age of 12, meaning his skeleton is aged 12, so he'll catch up later.

- For constitutional short stature, sometimes instead of mentioning bone age, they'll mention Tanner stage. For example, a 14-yr-old boy is shortest in his class + pubic hair is Tanner stage 2. The implication is he's still very early in development and will probably catch up.

- Bone age = chronologic age means genuine short stature. I've seen this in Turner syndrome Qs, where the female is usually < 5 feet.



- A mnemonic to remember the above sequence is "Tap em" (i.e., TAPM).

- Thelarche: Onset of breast development.

- Adrenarche: ↑ production of adrenal androgens, leading to the development of pubic and axillary hair.

- Pubarche: Pubic hair growth

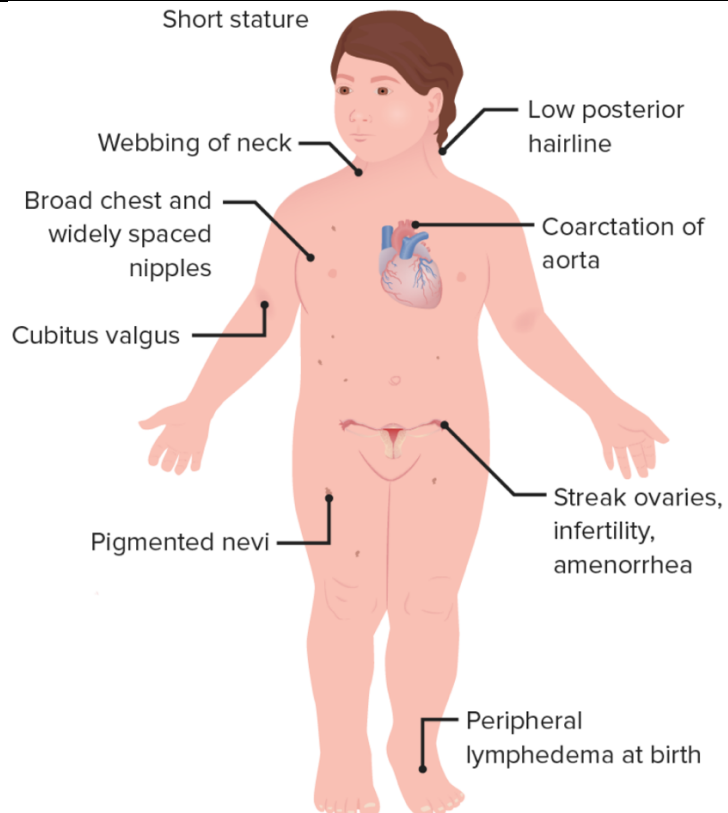
- Menarche: Onset of menstruation.

- USMLE asks straight-up what is most likely to occur first in a pre-pubescent female → answer = breast bud development.

Sex disorders

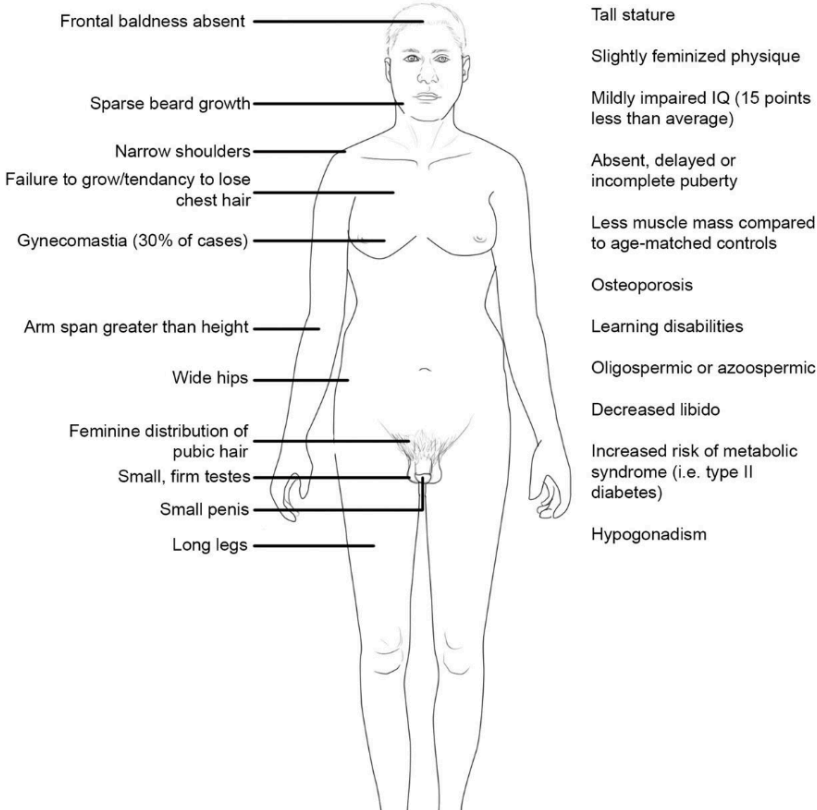
Short stature

Turner syndrome



- 45XO karyotype; female phenotype.

- Since there is only one X chromosome, the Q can say there is no Barr body visible on electron microscopy.

	<ul style="list-style-type: none"> - Infertile due to streak ovaries. In Turner, this is colloquially referred to as “menopause before menarche.” - Can still have children with IVF using donor egg + exogenous hormones (asked sometimes on behavioral/psych Qs). - LH and FSH both \uparrow due to primary hypogonadism (i.e., \downarrow negative-feedback at hypothalamus and anterior pituitary due to \downarrow ovarian hormones and inhibin). - Short stature (usually < 5 feet), Tanner stage 1 breast development (“shield chest”), cystic hygroma (webbed neck due to lymphatic insufficiency; asked on NBME); scattered nevi (confuses students for things like NF1, but I don’t know what to say; you need to know scattered nevi are seen in Turner); normal pubic and axillary hair (Tanner 4-5). - \uparrow risk of dysgerminoma developing from the streak ovaries; prophylactic oophorectomy is recommended, especially if there is Y-chromosome material present in rarer mosaic forms of Turner. - If Q tells you there’s a fraction of a female’s cells that are 46XX and another fraction that’s 45XO (i.e., somatic mosaic Turner), the answer for the mechanism is “post-fertilization mitotic error.” - Coarctation of the aorta + bicuspid aortic valve (aortic stenosis) HY.
Klinefelter syndrome	 <ul style="list-style-type: none"> - 47XXY karyotype; male phenotype. - Tall, eunuchoid body shape; small testes; gynecomastia; reduced IQ. - Q might say there is presence of electron-dense mass in the cell on electron microscopy (i.e., a Barr body). - Testes are present but are small; there is dysgenesis of the seminiferous tubules, leading to \uparrow LH and FSH due to \downarrow negative-feedback from \downarrow androgens and inhibin. - Estrogen/androgen ratio is \uparrow due to dysgenesis of Leydig cells (which make androgen). Absolute estrogen is also \uparrow due to \uparrow adipose tissue (therefore \uparrow aromatase). - \uparrow risk of breast cancer; risk of testicular cancer is only very subtly \uparrow, so prophylactic orchiectomy is not indicated.

Androgen insensitivity syndrome (AIS)	<ul style="list-style-type: none"> - 46XY karyotype; female phenotype. - Defect in androgen receptor. Since DHT is needed for external male development, the patient appears female. - Testosterone and DHT are normal or elevated due to ↓ negative-feedback at the hypothalamus and anterior pituitary → ↑ LH production → ↑ testicular androgen production. - The testes in AIS are usually located within the abdomen or inguinal canal. - Even though there is resistance to androgens, testes still develop because the <i>SRY</i> gene on the Y chromosome induces differentiation of the primitive gonads into testes. This differentiation isn't dependent on androgens. - The testes produce Müllerian-inhibitor factor, so there is no uterus or Fallopian tubes in AIS. - Even though the gonads also produce androgen, since we have resistance to it, the karyotypic male appears female (i.e., phenotypically female). - Breast development is Tanner 4-5 but pubic/axillary hair is Tanner 1. - USMLE vignette will say: 15-year-old girl is brought to the physician by her mother for not yet having a menstrual period + vagina ends in blind pouch + pubic/axillary hair is scant/absent → answer = AIS. - Next best step = ultrasound first if listed, then karyotype. - ↑ risk of testicular malignancy (dysgerminoma), so prophylactic orchiectomy is indicated after puberty (maximizes estrogen effects for phenotypic female development), unless evidence of malignancy is seen prior.
Müllerian agenesis	<ul style="list-style-type: none"> - Aka Mayer-Rokitansky-Küster-Hauser syndrome. USMLE will never assess this name, but students have asked about this before. - 46XX karyotype. - Presents identical to AIS on USMLE except they'll say pubic/axillary hair is normal/coarse. - In other words, 15-year-old girl + never had a menstrual period + vagina ends in blind pouch + pubic/axillary hair is coarse → answer = Müllerian agenesis. - Ovaries are present, since no Y chromosome is present (i.e., no <i>SRY</i> gene to convert primitive gonads into testes, so ovaries as the default ensue). - But since the Müllerian (paramesonephric) ducts don't develop, the Fallopian tubes, uterus, cervix, and upper vagina don't develop. - Next best step = ultrasound first if listed, then karyotype.
MIF deficiency	<ul style="list-style-type: none"> - Müllerian-inhibitory factor deficiency. - 46XY karyotype; phenotypically male with testes (i.e., internal and external structures are male), but failure of regression of the Müllerian ducts means a uterus, Fallopian tubes, cervix, and upper vagina are present. - The Müllerian structures are usually located in the pelvis between the bladder and rectum (similar to location for uterus in a female), or in the inguinal canal. They are often discovered incidentally during orchidopexy for cryptorchidism. - In other words, the Q can say there are undescended testes, where upon surgical reduction into the scrotum, a primitive uterus and Fallopian tubes are discovered.
5 α -reductase deficiency	<ul style="list-style-type: none"> - 46XY karyotype; phenotypically female, or neonate with ambiguous genitalia. - 5α-reductase is enzyme that converts testosterone → DHT. If there is a deficiency and DHT is ↓, male external structures don't develop, so phenotype is female. - Presents as "phallus (penis) at age 12." This is buzzy. They will say a 12-year-old girl has grown 4 inches in the past 4 months + has acne + hair on upper lip + clitoral hood is 3-4 cm → answer = 5α-reductase deficiency. - At puberty, the ↑↑ in testosterone can partially override the enzyme deficiency, leading to threshold production of DHT where male secondary sex characteristics can develop.
<i>SRY</i> gene translocation	<ul style="list-style-type: none"> - 46XX karyotype; phenotypically male.

	<ul style="list-style-type: none"> - The <i>SRY</i> gene from the Y chromosome is translocated usually onto one of the X chromosomes, resulting in formation of testes instead of ovaries. - The presence of testes leads to testosterone and DHT → develops male external structures; MIF production → no Müllerian structures develop. - Testes are usually small, and there can be penile abnormalities like hypo- or epispadias. - The USMLE will tell you a neonate appears male but is confirmed 46XX karyotype → answer = <i>SRY</i> gene translocation. - Rarely, this condition can be seen in 46XY karyotype, where the <i>SRY</i> gene is lost, rather than gained. Testes are absent, and instead there are streak ovaries + Müllerian structures.
Congenital adrenal hyperplasia (CAH)	<ul style="list-style-type: none"> - I discuss this in detail in the HY Arrows PDF. If you hate these conditions, you can go there for practice with the Qs I've written. - Ambiguous genitalia due to deficiency of 21-, 11-, or 17-hydroxylase in the adrenal glands. - If the Q says 17-OH substrates are high (i.e., 17-OH-pregnenolone or 17-OH-progesterone) and/or elevated DHEA-S or androstenedione, you know right away 17-hydroxylase deficiency is wrong, and the answer must be either 21- or 11-deficiency. - Then, if BP is low/normal or K^+ is high, the answer is 21-deficiency. - If BP is high or K^+ is normal/low, the answer is 11-deficiency. - 21-deficiency will basically present like Addison disease, where you get high K^+, low Na^+, low bicarb, and low pH. They can also say glucose is low due to low glucocorticoids. - Answer for mechanism of CAH on a 2CK NBME form for confirmed 46XX neonatal girl who has fused labia is "ACTH hypersecretion." In other words, the ↑ in adrenal androgens she has (i.e., DHEA-S in particular) can result from 21- or 11-hydroxylase deficiencies, where cortisol is ↓, so ACTH goes ↑ to compensate.
Swyer syndrome	<ul style="list-style-type: none"> - 46XY; phenotypically female. - Caused by failure of the primitive gonads to develop into testes, but they don't develop into ovaries either. They develop into streak gonads. - ↓ androgen production causes external female phenotype. Also leads to scanty/absent pubic/axillary hair. - Absence of MIF (since no testes) means Müllerian structures develop. - Presents similar to AIS – i.e., phenotypic female with scanty/absent pubic/axillary hair, but there are Müllerian structures (i.e., uterus, Fallopian tubes, cervix, and upper vagina) and ↓ androgens, whereas in AIS, Müllerian structures are absent and androgens are normal or ↑ (tissues are just insensitive to them).

Imperforate hymen	
<ul style="list-style-type: none"> - The hymen is a thin membrane that partially covers the vaginal opening in females. It normally has a small hole that allows the passage of menstrual blood out of the vagina. The size and shape of the hymenal opening can vary between females. - Imperforate hymen is when the hymen completely covers the vaginal opening, which can lead to hematocolpos and hematometra. 	
Hematocolpos	<ul style="list-style-type: none"> - Blood accumulation within the vaginal canal due to imperforate hymen. - USMLE Q will give a teenage girl who's never had a menstrual period. Physical exam shows a "blueish bulge" behind the hymen. The Q might say the girl has had monthly pain (i.e., she has in fact had menses, but blood is blocked from leaving the vagina due to the imperforate hymen). - Answer is either hematocolpos or "cruciate incision of the hymen."
Hematometra	<ul style="list-style-type: none"> - Blood backing up all the way to the uterus causing uterine distention.

	- Q will give what sounds like imperforate hymen + hematocolpos but you'll notice the blood pressure is low → distention of the uterus can trigger a vagal response leading to low BP.
--	--

HY Trisomy disorders	
Trisomy 21	<ul style="list-style-type: none"> - Down syndrome; caused by having 3 chromosome 21s, instead of the normal 2. - 95% due to extra chromosome 21 as a result of meiotic nondisjunction in advanced maternal age (1 in 350 at age 35; 1 in 100 at age 40; 1 in 10 at age 50). - 4% due to Robertsonian translocation – i.e., obscure process where long arm of chromosome 21 attaches to another chromosome (usually 14) and is passed to conceptus along with two normal chromosome 21s; the result is the conceptus inherits 3 chromosome 21s. - 1% is mosaic Down, which is due to post-fertilization mitotic (not meiotic) error. In this case, not all cells of the conceptus contain the trisomy. - Most common genetic cause of mental retardation; second most common genetic cause is Fragile X. Most common cause of mental retardation overall is fetal alcohol syndrome. - Associated with flattened facies; slanted palpebral fissures; epicanthal folds; single palmar crease (this finding non-specific but still often mentioned in Down); large gap between the first and second toes; Hirschsprung disease; duodenal atresia (double bubble sign on AXR); endocardial cushion defects (AVSD, VSD, or ASD); pulmonary artery malformations; acute lymphoblastic leukemia; congenital hypothyroidism; Eustachian tube atresia; Brushfield spots (iris lesions). - First trimester tri-screen (8-10 weeks): ↑ nuchal translucency, ↑ hCG, ↓ PAPP-A. Students often remember something is abnormal about PAPP-A, but they forget the direction, so remember that it's ↓, not ↑. - Although not technically part of the tri-screen, a hypoplastic nasal bone is also an important finding in Downs (reflects flattened facies). - Second-trimester quad screen (↓ AFP, ↑ hCG, ↓ estriol, ↑ inhibin A). As discussed earlier, just remember that the ones that have "Hs" are ↑ (i.e., hCG and inhibin A both have Hs, so those are the ones that are ↑).
Trisomy 18	<ul style="list-style-type: none"> - Edward syndrome. - Low-yield for USMLE. But you have to know it exists. - Low-set ears; prominent occiput; rocker-bottom feet; clenched hands / overlapping fingers; omphalocele or gastroschisis. - Some students get emotional about the Edward and Patau syndrome quad screens, but USMLE doesn't give a fuck. But in theory the arrows are all ↓. - Usually fatal <i>in utero</i> or shortly after birth.
Trisomy 13	<ul style="list-style-type: none"> - Patau syndrome. Rare as fuck. - Holoprosencephaly (cylopia) / failure of halves of brain to separate; polysyndactyly. - Quad screen arrows all ↓, except inhibin normal. USMLE doesn't care though. - Usually fatal <i>in utero</i> or shortly after birth.

Oligo- vs polyhydramnios	
Polyhydramnios	<ul style="list-style-type: none"> - Excessive amniotic fluid. - Important maternal causes: <ul style="list-style-type: none"> - GDM. As discussed before, ↑ glucose in the fetus pulls water with it through the fetal kidneys, causing ↑ urinary volume. - Fetal hypoxia. This could be due to maternal anemia, HDN, or infections like Parvo. If there is ↓ oxygen delivery from the mom, fetal RBC hemolysis, or ↓ fetal RBC production, the fetal hypoxia results in a compensatory ↑ in fetal cardiac output in an attempt to oxygenate tissues. One way this is accomplished is by dilating the renal vessels, which lowers resistance on the

	<p>peripheral vasculature, but it also simultaneously increases renal blood flow and urine production.</p> <ul style="list-style-type: none"> - Multiple gestation pregnancies. This is due to combined \uparrow urinary output in the setting of multiple fetuses. - Important fetal causes: <ul style="list-style-type: none"> - Fetal hydrops (severe edema in the fetus usually as a result of heart failure). In the setting of Parvo B19 infection, fetal anemia, or HDN, cardiac output \uparrow to compensate, leading to \uparrow renal perfusion and \uparrow urine production. In the setting of fetal heart failure where cardiac output is \downarrow, \uparrow venous pressure will cause edema, where the kidneys attempt to rid the body of excess fluid by \uparrow urinary output.
Oligohydramnios	<ul style="list-style-type: none"> - Insufficient amniotic fluid. - Important maternal causes: <ul style="list-style-type: none"> - Uteroplacental insufficiency. Reduced blood flow to the fetus as a result of smoking, preeclampsia, and SLE (discussed in below tables) can result in compromised renal function and urinary output. This is likely related to impaired nutrient delivery in the setting of minimally sufficient oxygenation, where renal cardiac output does not increase (since oxygenation is sufficient), but nutrient delivery is low (so renal function is reduced). - Important fetal causes: <ul style="list-style-type: none"> - Posterior urethral valves. Most common genitourinary abnormality in neonatal males. "Posterior" refers to the prostatic urethra developing thin membranes, or "valves," that prevent urinary outflow. This can lead to obstructive uropathy with vesicoureteral reflux and hydronephrosis. Severity can vary; some Qs give severe oligohydramnios; other Qs are male neonate hours old who hasn't urinated, or male neonate weeks old with urinary retention. - Renal agenesis (Potter sequence). Failure of kidney development \rightarrow \downarrow urine output \rightarrow \downarrow amniotic fluid \rightarrow \downarrow swallowing of fluid by fetus \rightarrow impaired lung development \rightarrow pulmonary hypoplasia. The \downarrow amniotic fluid also leads to flattened facies and rocker-bottom feet.

SLE and antiphospholipid syndrome

- SLE causes uteroplacental insufficiency and recurrent miscarriage when patient has anti-phospholipid antibodies. The latter result in microthrombi within uteroplacental microvasculature leading to decreased blood flow and fetal compromise. If miscarriage does not occur, intrauterine growth restriction (IUGR) and oligohydramnios may result secondary to the reduced uteroplacental oxygen delivery.
- Women with Hx of miscarriage due to phospholipid syndrome in SLE are treated with combination therapy of low-dose aspirin + LMWH in subsequent pregnancies. Warfarin is avoided because it is teratogenic.
- SLE resulting in uteroplacental insufficiency is a risk factor for preeclampsia, since the latter is caused by reduced uteroplacental perfusion.
- IUGR in pregnancy is best ascertained by looking at fetal abdominal circumference. Sounds weird (i.e., student says, "Why not head circumference or something."), but it's because abdominal circumference reflects liver size and overall fetal fat accumulation, which are notably affected in IUGR. When the placenta is not delivering adequate oxygenation and nutrients, the fetus often prioritizes brain over abdominal growth, leading to a reduced abdominal circumference.

HY organ system infections	
Pyelonephritis	<ul style="list-style-type: none"> - USMLE wants you to know pregnant women are at ↑ risk of pyelo due to two main reasons: - 1) Progesterone slows ureteral peristalsis, thereby ↑ risk of urinary stasis and backup to kidney. - 2) Compression of ureter(s) by uterus, notably in 3rd trimester, ↑ risk of stasis. - For this reason, asymptomatic bacteriuria is always treated in pregnancy, even though it is not treated in non-pregnant women. Nitrofurantoin is a classic drug used to treat asymptomatic bacteriuria, standard UTIs, and cystitis in pregnancy.
Cholecystitis	<ul style="list-style-type: none"> - Progesterone also slows biliary peristalsis, ↑ risk of biliary sludging and cholesterol stone formation. - Estrogen upregulates HMG-CoA reductase, ↑ hepatic cholesterol synthesis, thereby ↑ risk of stone formation. - Cholelithiasis will present as colicky epigastric pain, usually after meals. - Cholelithiasis + fever = cholecystitis. - Diagnose both with ultrasound. - For cholecystitis only, if it is strongly suspected by ultrasound is negative, the next best step is HIDA scan. - Ursodeoxycholic acid (ursodiol) can be given to pregnant women with cholelithiasis to ↓ stone size. The MOA of this drug is: ↓ cholesterol secretion into bile. - Laparoscopic cholecystectomy is done for cholecystitis in pregnancy.
Appendicitis	<ul style="list-style-type: none"> - Highest yield point is that appendicitis can present as RUQ pain in pregnancy because the uterus pushes the appendix upward. - The Q will say ultrasound of the gallbladder shows no abnormalities, which is how you know the RUQ pain is not due to cholecystitis. - Laparoscopic appendectomy is performed in pregnancy.

Other HY Obgyn infections	
Chorioamnionitis	<ul style="list-style-type: none"> - Infection of the uterus during pregnancy. - Greatest risk factor is ROM >18 hours. - Cause is usually polymicrobial. - Tx = ampicillin + gentamicin +/- clindamycin.
Endometritis	<ul style="list-style-type: none"> - Infection of the uterus <i>after</i> pregnancy. - Endometritis = "Postpartum endometritis" for all intents and purposes. - Can present as fever, uterine tenderness, and foul-smelling lochia within a few days of delivery. - Cause is usually polymicrobial. - Q will say woman had C-section two days ago + now has fever + lower abdo pain +/- foul-smelling lochia → answer = postpartum endometritis; chorioamnionitis is wrong answer because she's not pregnant anymore. - Tx = ampicillin + gentamicin +/- clindamycin. - USMLE also wants you to be aware of what is "normal post-operative course" versus endometritis. For example, the NBME Q can say something like, woman had Caesar two days ago + temp 99.3 F + incision site mildly erythematous + two inguinal lymph nodes are palpable and tender → answer = "normal post-operative course." Surgery is trauma, and the immune system will generate a natural response to it. Palpable lymph nodes can be a normal response to inflammation and surgery.
Septic pelvic thrombophlebitis	<ul style="list-style-type: none"> - Formation of infected blood clots in the pelvic veins (umbrella term for uterine and ovarian veins). - Endometritis is big risk factor. - Differentiated from endometritis in that it causes persistent pelvic pain and fever despite administration of antibiotics. - Answer choice shows up quite a bit on 2CK forms, so know it exists.
Puerperal sepsis	<ul style="list-style-type: none"> - Generalized term for sepsis occurring after childbirth.

	<ul style="list-style-type: none"> - Presentation is variable; causes high fever, chills, tachycardia, and low BP. - Q might list both puerperal sepsis and septic pelvic thrombophlebitis as answer choices. Remember that SPT is pelvic pain unresponsive to antibiotics; puerperal sepsis is actual sepsis due to a number of causes, but often endometritis.
Toxic shock syndrome	<ul style="list-style-type: none"> - Caused by TSST superantigen of <i>S. aureus</i>. - Tampon use, or vulvovaginal/perineal skin infections are HY etiologies. For non-Obgyn Qs, cotton nasal packing also HY. - Toxin bridges MHC-II on macrophages with T cell receptor on CD4+ T cells, causing macrophages to release cytokines leading to shock. - Shows up on 2CK material where they ask most likely cause of death in TSS, and the answer is ARDS. Slightly unusual answer, but I don't know what to tell ya.

Peripartum bleeding for IM	
Uterine atony	<ul style="list-style-type: none"> - Most common cause of postpartum bleeding (70-80%). - Presents as vaginal bleeding in the context of large, boggy uterus. - Uterine massage immediately following Stage 2 delivery ↓ risk. - Refractory bleeding can be treated oxytocin to enhance uterine tone and contractions. If ineffective, ergonovine/methylergonovine can be administered. - Surgery such as uterine artery embolization or hysterectomy is last resort. - Ergonovine is contraindicated in HTN, preeclampsia, migraine with aura, smokers, and cardiovascular disease.
Vaginal laceration	<ul style="list-style-type: none"> - Usually seen in the setting of fetal macrosomia (e.g., maternal diabetes), as discussed earlier. - Episiotomy can be performed to ↓ risk.
Placenta previa	<ul style="list-style-type: none"> - Placenta implants over the internal cervical os. - Causes painless 3rd trimester bleeding. - C-section recommended 37 weeks onward. - Prior to 36 weeks, placental implantation site can occasionally move off the cervical os as the uterus continues to grow. - Hx of prior interventions to the uterus (i.e., myomectomy, previous Caesars) ↑ risk of placenta previa due to ↑ probability of abnormal implantation (i.e., if the endometrial lining is disrupted in any form, then chance of normal implantation is ↓).
Abruptio placentae	<ul style="list-style-type: none"> - Placenta detachment from the uterine wall prior to parturition. - Causes painful 3rd trimester bleeding. - Can present as intense cramping. - Classic causes are cocaine and deceleration injury (i.e., car accident).
Placenta accreta	<ul style="list-style-type: none"> - Placental attachment to the surface of the myometrium. - Causes postpartum bleeding.
Placenta increta	<ul style="list-style-type: none"> - Placental attachment into the myometrium. - Causes postpartum bleeding.
Placenta percreta	<ul style="list-style-type: none"> - Placental attachment through the myometrium, sometimes onto adjacent structures such as the bladder (percreta = perforates). - Causes postpartum bleeding.

Fetal non-stress testing	
Accelerations	<ul style="list-style-type: none"> - The non-stress test (NST) is a test that monitors fetal heart rate. - Accelerations reflect fetal well-being and refer to an increase in fetal heart rate of ~20 bpm that lasts ~20 seconds. This should occur 2-3 times within a 20-minute period.

Early decelerations	<ul style="list-style-type: none"> - Mean fetal head compression. - Drop in the fetal heart rate at the same as uterine contractions (i.e., the nadir of the fetal bradycardia and peak of uterine contraction are in same y-plane). - Drop in fetal HR occurs as a result of \uparrow vagal outflow. This is in part due to \uparrow vascular resistance as a result of the compression. <p>Fetal heart rate</p> <p>Contractions</p> <p>Min</p> <p>Early deceleration Late deceleration Variable deceleration</p>
Late decelerations	<ul style="list-style-type: none"> - Mean fetal hypoxia, or uteroplacental insufficiency. - The fetal bradycardia occurs just after the uterine contraction. - Late decels are the “bad type.” - Treatment for both late and variable decels is triad of 1) stop all oxytocin; 2) give maternal oxygen; 3) position the patient left-lateral decubitus. - If the above measures don't work, C-section is often performed. - Fetal scalp pH can be done in theory to assess degree of fetal hypoxia if decels are prolonged. Procedure involves obtaining a fetal blood sample from the scalp. If pH of the fetal blood is <7.2, this suggests acidosis and hypoxia. Even though <7.35 is acidosis, the <7.2 cutoff is used as a stronger threshold to determine whether more urgent interventions are warranted.
Variable decelerations	<ul style="list-style-type: none"> - Mean umbilical cord compression. - Amnioinfusion is an answer on USMLE as Tx for variable decelerations in conjunction with above triad. This is when sterile saline is injected into the uterine cavity to help relieve umbilical cord compression.

Sheehan syndrome

- Maternal pituitary grows in size during pregnancy due to \uparrow hormone production.
- Traumatic labor (e.g., C-section with loss of considerable blood) \uparrow risk of anterior pituitary ischemic infarction.
- Textbook vignette is \downarrow ability to breastfeed due to \downarrow milk production following labor where BP was \downarrow .
- Schools/resources will usually just teach that prolactin is \downarrow . But USMLE wants you to know that **all hormones** coming from the anterior pituitary are low.
- NBME wants a \downarrow for prolactin, ACTH, and TSH, as well as an \uparrow for aldosterone.
- The \uparrow for aldosterone is weird, I agree. Take it up with NBME, not me. My suspicion is that \downarrow cortisol from \downarrow ACTH can lead to \downarrow basal blood pressure, where aldosterone could go \uparrow to compensate. The patient is not going to have overt hyperaldosteronism with \uparrow Na^+ , \downarrow K^+ , \uparrow HCO_3^- , and \uparrow pH. It's more that, in theory, basal level aldosterone could go \uparrow slightly to compensate.
- The vignette can mention fatigue, which reflects \downarrow TSH (secondary hypothyroidism).

HY repro-cardio DDx for IM	
Amniotic fluid embolism	<ul style="list-style-type: none"> - The answer on USMLE for acute-onset shortness of breath and tachycardia 30 seconds to 2 minutes after delivery of the placenta. - Amniotic fluid leaks into maternal circulation + goes to pulmonary arterioles. - Can cause disseminated intravascular coagulation with bleeding from IV lines / catheter sites. - Tx = supportive.
Pulmonary embolism	<ul style="list-style-type: none"> - The answer on USMLE for acute-onset shortness and tachycardia two days postpartum when the mother gets up to go to the bathroom (presumably a DVT that formed while in hospital bed launched off to lungs). - Tx = heparin first, followed by CT of the chest (aka spiral CT or CT angio). - <i>If woman is pregnant</i>, then do V/Q scan before CT. This is in order to decrease potential radiation exposure to the fetus. - If V/Q scan is performed during pregnancy that shows "segmental perfusion defects" (i.e., suggestive of PE), the next best step in diagnosis is CT of the chest if it's listed. Student says, "Wait, but I thought you just said we don't do that in pregnancy because of radiation." I agree with you. That's why we did V/Q scan first. But if they force you to choose a NBS in Dx following the V/Q scan, the answer is still CT. Take it up with USMLE, not me.
Peripartum cardiomyopathy	<ul style="list-style-type: none"> - Dilated cardiomyopathy almost always during 3rd trimester or in the first few months postpartum. - Cause is multifactorial, but some studies have identified an autoantibody-mediated process. - Will present as gradually worsening shortness of breath on exertion (i.e., LHF at a minimum). Depending on severity, can also present with JVD and significant pitting edema (RHF findings). - Peripartum cardiomyopathy tends to get worse with each subsequent pregnancy. - Diagnosis is made with transthoracic echo looking for low ejection fraction. - Qs like to ask how to determine degree of maternal/fetal risk in subsequent pregnancies → answer = transthoracic echo (looking for EF). In other words, the next pregnancy is going to have an even lower EF than the current, so if the EF is already significantly low (NR 55-70%), we know it'll only be worse subsequently.
Normal peripheral edema	<ul style="list-style-type: none"> - Peripheral edema is common in pregnancy due to ↑ plasma volume + the uterus compressing the pelvic veins and IVC; both cause ↑ venous hydrostatic pressure.
Atelectasis	<ul style="list-style-type: none"> - Confusing word that refers to "lung collapse," or "collapse of alveoli." - Highest yield point for USMLE is that it is the most common cause of fever within 24 hours of post-surgery. If this is the first time you're reading this, that might sound weird, but this is pass-level and extremely important for 2CK. - There is one 2CK Q where they say a woman had a C-section two days ago and the answer was still atelectasis, so even though it's most common <24 hours, just be aware one Q exists where, oh em gee, it's 2 days later. - The mechanism is related to combo of pain meds + sedation, where breathing becomes slower + shallower in hospital bed, leading to mild collapsing of some alveoli. This is why breathing exercises can be important post-surgery. - Will often present as bibasilar shadows or opacities. In other words, patient had surgery yesterday + now has fever + CXR shows mild opacity at the lung bases → answer = atelectasis. - NBME assesses obstructive (aka resorptive) atelectasis. This is when an area of lung distal to an obstruction from, e.g., a tumor, can cause alveoli to collapse. This then increases the chance for pneumonia distal to the obstruction. - 2CK IM form has "endobronchial obstruction" as answer for distal area of lung collapse (i.e., atelectasis) in patient with lung cancer; "vascular occlusion by tumor" is wrong answer (makes sense, as the tumor obstructs the respiratory tree, not blood vessel, in this case, but I've seen students accidentally choose the latter).
Budd-Chiari syndrome	<ul style="list-style-type: none"> - Hepatic vein thrombosis due to hypercoagulable state in pregnancy.

	<ul style="list-style-type: none"> - Presents as abdominal pain + hepatomegaly +/- ascites (latter indicates hydrostatic pressure backup to the portal vein). - Placenta produces plasminogen-activator inhibitor (PAI-2), which ↓ plasmin activity and fibrinolysis → hypercoagulable state. In addition, ↑ estrogen and progesterone contribute to hypercoagulable state by ↑ fibrinogen, clotting factor, and vWF synthesis. - Hypercoagulable state in pregnancy is an evolutionary mechanism to ↓ hemorrhage risk at parturition.
Hemorrhoids	<ul style="list-style-type: none"> - Bleeding or protrusion from rectal veins. - Common during pregnancy, particularly in the second and third trimesters. - ↑ Pelvic blood flow and pressure from uterus on the pelvic and rectal veins. - ↑ Progesterone during pregnancy relaxes the walls of the veins, allowing them to swell more easily. - Constipation, which is also common during pregnancy, can cause straining during defecation, further contributing to the development of hemorrhoids. - Tx = dietary modifications to prevent constipation, using cushions or pillows to relieve pressure when sitting, and avoiding prolonged periods of standing or sitting.

Polycystic ovarian syndrome (PCOS)	
	<ul style="list-style-type: none"> - High BMI female → insulin resistance. - Insulin resistance causes abnormal GnRH pulsation → leads to ↑ LH and ↓ FSH. This is often truncated as just saying there's an ↑ LH/FSH ratio. Some students think FSH is also ↑, but it's just the ratio that's ↑. That's wrong. FSH is low. - LH normally acts on the theca lutein cells of the ovaries to make androgens. Since LH is ↑, we get hirsutism. - FSH normally stimulates follicular development. Since FSH is ↓, we have poor follicular development, leading to failure of a Graafian follicle to rupture during ovulation. The unruptured follicle is retained as a follicular cyst. - Failure of ovulation is called anovulation. This term is exceedingly HY on USMLE. It presents as a female with irregular periods. - Anovulation is a broader term than PCOS, as it can be due to other conditions as well, such as hypothyroidism and Cushing syndrome. But when you hear the word "anovulation" alone, it is usually used as synonymous for the same mechanism as PCOS – i.e., high-BMI female who has irregular periods due to abnormal GnRH pulsation causing an ↑ LH/FSH ratio, with the ↓ FSH causing failure of follicular rupture. - So high-BMI female + irregular periods = anovulation till proven otherwise. - Anovulation + hirsutism = PCOS. - In clinical practice, part of the PCOS diagnosis requires ultrasounds showing 11+ cysts bilaterally (Amsterdam criteria). But USMLE doesn't assess this. You just need to know anovulation + hirsutism = PCOS. - Normally when a follicle ruptures, the remnant is called the corpus luteum, which secretes progesterone. - Progesterone inhibits growth of endometrium; estrogen stimulates growth of endometrium. - Women who have anovulation have ↓ progesterone production because they don't form a corpus luteum. - This means they have ↑ estrogen in comparison to progesterone. We call this unopposed estrogen. This is one of the highest yield phrases for USMLE. - Unopposed estrogen means ↑ risk of endometrial hyperplasia and, in turn, ↑ risk of endometrial carcinoma. - The Q can give you a high-BMI female who's post-menopausal + has vaginal bleeding. Answer is just straight-up endometrial biopsy. Student asks how we know it's endometrial cancer. My response is, if she's overweight, this implies she was probably overweight in the past, which implies she's had history of anovulatory cycles and endometrial hyperplasia, leading to ↑ endometrial cancer risk. - Because insulin resistance is the basis for PCOS, patients are at ↑ risk of developing type II diabetes. - As mentioned above, hypothyroidism and Cushing syndrome are also HY causes of anovulation on USMLE. - ↑ Glucocorticoids in Cushing syndrome can cause insulin resistance and anovulation, where the diagnosis can appear like PCOS. The difference is PCOS is idiopathic in response to high BMI – i.e., it is not caused by a known secondary etiology like Cushing syndrome, even though the presentations can be similar.

- Hypothyroidism leads to ↑ thyroid-releasing hormone (TRH), which stimulates prolactin, which causes abnormal GnRH pulsation. Even though this is the mechanism, the caveat I issue is that USMLE does not directly assess this, and it is infinitely more important you know that the mechanism for prolactin secretion is ↓ dopamine, or overt dopamine-2 receptor antagonism (i.e., for severance of pituitary stalk Qs).

Progesterone withdrawal test

- Progesterone withdrawal test is the process of giving progesterone followed by seeing if bleeding occurs following its withdrawal. It can be used to help diagnose the cause of oligo- or amenorrhea.
- As discussed earlier, menses are caused by the presence of progesterone followed by its withdrawal.
- If bleeding occurs (i.e., positive progesterone withdrawal test), it means estrogen levels are normal and the endometrial lining builds up just fine, and that anovulation is the cause of the irregular menses.
- In PCOS, for instance, since we don't have a corpus luteum and progesterone secretion, we don't have the sequence of "progesterone present followed by withdrawal," so we can't get regular menses. However, since estrogen levels are normal in PCOS, the endometrial lining can grow without a problem, so if progesterone is given exogenously, followed by its withdrawal, we will see bleeding.
- In conditions like Turner (where estrogen is low) or Asherman (scarred uterus that can't grow), giving progesterone won't induce bleeding since the endometrial lining hasn't developed. The bleeding will only occur if estrogen is present in normal amounts to allow for endometrial growth, where the administration, followed by withdrawal, of exogenous progesterone essentially induces forced menses.

Primary dysmenorrhea vs endometriosis vs adenomyosis

Primary dysmenorrhea	<ul style="list-style-type: none"> - Dysmenorrhea = period pain. - Primary dysmenorrhea = "normal period pain"; benign. - Mechanism is prostaglandin PGF2α hypersecretion. - During menstruation, the endometrial cells release high levels of prostaglandins, which cause uterine contractions and pain. The prostaglandins can also make their way into the systemic circulation, leading to headache and nausea. - This is the answer on USMLE for period pain under the age of 20. The Q can say, girl who is 17 has menstrual pain so bad she has to miss class + physical exam shows no abnormalities → answer = primary dysmenorrhea. - The answer can also be written simply as "prostaglandin secretion." - The key detail regarding primary dysmenorrhea is that the physical exam is normal. - In endometriosis, the physical exam is abnormal + is always over age 20. - Treatment is NSAID. OCP is wrong answer if listed alongside NSAID (on NBME).
Endometriosis	<ul style="list-style-type: none"> - Growth of endometrial tissue outside the uterus. Most common location is the ovary, but can also grow in other locations like the pouch of Douglas. - Mechanism is thought to be retrograde menstrual flow through the Fallopian tubes + seeding onto the ovaries or peritoneum. - Causes severe menstrual pain over age 20 + an abnormal physical exam. - The abnormal physical exam can be any miscellaneous finding – i.e., there is no specific finding you have to memorize. They can say findings such as nodularity of the uterosacral ligaments, a fixed retroverted uterus (due to adhesions from lesions), or pelvic tenderness. - In contrast, severe period pain + normal physical exam = primary dysmenorrhea. - In other words: <ul style="list-style-type: none"> - 23F + period pain so bad she has to miss work + normal physical exam → answer = prostaglandin secretion / primary dysmenorrhea. - 23F + period pain so bad she has to miss work + physical exam shows nodularity of the uterosacral ligaments → answer = endometriosis. - Descriptors such as pain with defecation (due to pouch of Douglas lesions) or dyspareunia (pain during sex) are highly buzzy and pass-level but too easy, so are often omitted from NBME questions, as per my observation.

	<ul style="list-style-type: none"> - USMLE wants diagnostic laparoscopy as next best step. - NSAIDs and OCPs are short-term measures, but definitive Tx is laparoscopic removal of lesions.
Adenomyosis	<ul style="list-style-type: none"> - Growth of endometrial tissue within the myometrium. - Presents as a diffusely enlarged uterus + vaginal bleeding in woman 30s-50s. - May or may not be painful. - Q will say woman had tubule ligation two years ago + now has uterus that is 8 weeks' gestation in size + vaginal bleeding → answer = adenomyosis. Student is confused and says "how can she be pregnant if she had tubule ligation?" She's not. Use your head. It's just how the Q can describe the ↑ size. - Tx = NSAIDs + OCPs. - Leuprolide can be used in theory, but I haven't seen it assessed.

Other repro/obgyn terms	
Mittelschmerz	- Ovulatory pain; can present as sharp adnexal pain mid-cycle.
Menorrhagia	- Heavy periods (>80 mL; can present with clots); and/or menses lasting >7 days.
Metrorrhagia	<ul style="list-style-type: none"> - Mid-cycle bleeding (i.e., any bleeding between periods). - Slightly different from "breakthrough bleeding," which refers to mid-cycle bleeding in women using hormonal contraception.
Dyspareunia	- Persistent or recurrent pain during sex; no one specific etiology.
Vaginismus	- Dyspareunia specifically caused by involuntary contraction of the pelvic floor muscles, especially the pubococcygeus (PC), presenting as spasmodic pain during sex.

Miscellaneous repro/obgyn Ddx for IM	
Asherman syndrome	<ul style="list-style-type: none"> - Scarring of the uterus by fibrous adhesions, aka uterine synechiae. - Caused by Hx of instrumentation – i.e., D&C. - Can cause amenorrhea.
Cervical stenosis	<ul style="list-style-type: none"> - Q will say female has a Hx of LEEP for cervical CIN2 or 3 six months ago + now has pelvic pain with menses + examination shows a small, scarred cervical os. - Pain can occur in theory if outflow of menses is ↓, similar to imperforate hymen.
Ovarian hyperstimulation syndrome (OHSS)	<ul style="list-style-type: none"> - Can occur in some women who take fertility meds (e.g., clomiphene) to stimulate egg production. - Results from over-response to the drug, leading to swelling of the ovaries and fluid accumulation in the abdomen, sometimes also affecting the chest. - Symptoms of OHSS can range from mild (i.e., bloating and mild pain) to severe, involving rapid weight gain, severe pain, and shortness of breath. - Usually self-limiting / self-resolves. Just know the Dx exists.
Premature ovarian failure	<ul style="list-style-type: none"> - Aka primary ovarian insufficiency. - Term used to apply to idiopathic menopause age 40 or younger.
Atrophic vaginitis	<ul style="list-style-type: none"> - Vaginal atrophy, leading to thin, dry, itchy, and inflamed vaginal walls. - Usually due to menopause, but can in theory be caused by any etiology of low estrogen. - Can cause dyspareunia. - Topical lubricants are tried first, followed by topical estrogen.
Chemo- / radiotherapy-induced amenorrhea	<ul style="list-style-type: none"> - As the name implies. You just need to be aware that chemo- and radiotherapy can cause amenorrhea. - Shows up on NBME as "primary hypogonadism" as the answer – i.e., the ovaries themselves are hypo-secreting hormones as reason for amenorrhea.
Autoimmune oophoritis	- Idiopathic autoantibody-mediated destruction of ovarian tissue in women of child-bearing age. Rare. Just know it exists.

Carpal tunnel syndrome	<ul style="list-style-type: none"> - Compression of median nerve within carpal tunnel. - Normal in pregnancy due to edema in 2nd and 3rd trimesters.
Chronic interstitial cystitis	<ul style="list-style-type: none"> - Unexplained pelvic pain, bladder pain, and/or dysuria >6 weeks, where all laboratory studies are normal. - Can present with anterior vaginal wall pain (bladder is anterosuperior to vagina). - Q will say 25F + 6 months of dysuria + pubic pressure + pregnancy test negative + labs all normal → Dx = interstitial cystitis straight-up. Not hard. - Treatment is mundane, soft porn stuff like lifestyle modification and dietary changes. Steroids are a wrong answer.

Notable Teratogens	
<ul style="list-style-type: none"> - Agent that causes malformations in the fetus. - Not an exhaustive list. Point is to be HY, not superfluous. - Fetus is most susceptible at 3-8 weeks' gestation. 	
Agent	Defect(s) in the fetus
ACE inhibitors	- Renal issues.
Aminoglycosides	- Hearing issues.
Anti-epileptics	<ul style="list-style-type: none"> - Neural tube defects (disrupt folate metabolism). - Fetal hydrantoin syndrome (fingernail/digital hypoplasia, facial anomalies).
Carbimazole/methimazole	- Aplasia cutis congenita, choanal atresia, esophageal atresia.
Diethylstilbestrol (DES)	- Vaginal clear cell carcinoma 30-40 years later.
Isotretinoin	- Craniofacial and cardiac abnormalities; cleft lip/palate.
Lithium	- Ebstein anomaly (atrialization of right ventricle).
Methotrexate	- Neural tube defects.
NSAIDs	- Premature closure of ductus arteriosus; oligohydramnios; inhibited labor.
Ribavirin	- Craniofacial anomalies; growth deficits.
Tetracyclines	- Fetal teeth discoloration; inhibition of bone growth.
Thalidomide	<ul style="list-style-type: none"> - Phocomelia (severe flipper-like malformation of limbs). - Was used frequently in the 1950s-60s to treat nausea in pregnancy.
Warfarin	<ul style="list-style-type: none"> - Bone and facial anomalies. - CNS defects like Dandy-Walker malformation (HY Neuroanatomy PDF). - Bleeding diathesis in fetus.

Substance abuse in pregnancy	
Agent	Defect(s) in the fetus
Alcohol	<ul style="list-style-type: none"> - Fetal alcohol syndrome; most common cause of mental retardation. - Heart/lung defects (defective neural crest migration). - Smooth, flat, and/or elongated philtrum. - Thin vermilion border (thin upper lip). - Widely spaced eyes (hypertelorism), midface hypoplasia, short nose.
Amphetamines + cocaine	<ul style="list-style-type: none"> - IUGR; cognitive deficits. - NBME can give long vignette of drug use, followed by ask what is most likely to occur in the pregnancy → answer = "preterm delivery and birth." Sounds non-specific and vague, but it's still <i>most likely</i> in comparison to most other things. - Cocaine in particular also increases risk of abruptio placentae.
Anti-epileptics	<ul style="list-style-type: none"> - Neural tube defects (disrupt folate metabolism). - Fetal hydrantoin syndrome (fingernail/digital hypoplasia, facial anomalies).
Heroin/opioids	<ul style="list-style-type: none"> - Neonatal heroin/opioid withdrawal. - Piloerection (goosebumps), yawning, rhinorrhea.
MDMA (ecstasy)	- IUGR; cognitive deficits.

Smoking	- IUGR and reduced IQ.
---------	------------------------

Contraception	
Barrier (condoms)	<ul style="list-style-type: none"> - Sheaths made of latex, polyurethane, or lambskin worn over the penis (male condom) or inside the vagina (female condom). - Self-explanatory, but apart from abstinence, male condoms are #1 way to ↓ pregnancy and STD risk. - Recommended for use in women on isotretinoin, even if they are already on other contraceptive method. - OCPs ↑ risk of cervical cancer slightly, not as a direct effect, but because of ↓ barrier contraception use, where HPV exposure is ↑.
Combined oral contraceptive pills	<ul style="list-style-type: none"> - Contain both estrogen and progesterone. - Estrogen helps to ↓ breakthrough bleeding risk (i.e., metrorrhagia). - Estrogen ↓ probability of ovulation; progesterone ↓ penetration of sperm by ↑ thickening of cervical mucous. In some women, and depending on dose, progesterone can also ↓ ovulation. - Contraindicated in smokers >35 (HY on USMLE), migraine with aura, Hx of thrombotic disorders, or current breast/gynecologic cancer due to the estrogen-containing component. - 2CK forms can be nebulous and, rather than writing OCPs as the answer, they can write "synchronization of endometrium," or "triphasic oral contraceptive pills," which mean the same thing. - ↓↓ Risk of ovarian cancer the most due to synchronization of cycles (asked on NBME). Also ↓ risk of endometrial (probably also due to synchronization). - ↑ risk of cervical cancer due to ↓ barrier contraception use (as mentioned above); some studies have suggested slight ↑ in breast cancer risk, albeit without significance.
Progestin-only pills	<ul style="list-style-type: none"> - Aka "mini-pill"; only contain progesterone analogue. - Thicken cervical mucous. - Must be taken precisely at same time every day, so require female is well-adherent / compliant.
Transdermal patch	<ul style="list-style-type: none"> - Releases both estrogen and progesterone and acts same as combined OCP. - Worn for one week at a time.
Vaginal contraceptive ring	<ul style="list-style-type: none"> - Aka NuvaRing; releases both estrogen + progesterone. - Worn monthly.
Copper IUD	<ul style="list-style-type: none"> - Copper intrauterine device; releases (you wouldn't have guessed it) copper ions into the uterine cavity, creating an environment that is toxic to sperm + inhibits their motility, thereby preventing fertilization. - Known for being one of the most effective forms of emergency contraception when inserted within five days post-coitally and can provide up to 10 years of contraceptive protection. - IUDs have risk of migration through uterine wall.
Levonorgestrel IUD	<ul style="list-style-type: none"> - Release progesterone analogue; usually last 3-7 years and are ideal in women who desire longer-term contraception or have poor medication compliance. - Thicken cervical mucous. - IUDs have risk of migration through uterine wall.
"Depo shot"	<ul style="list-style-type: none"> - Depot medroxyprogesterone acetate injection form of contraception. - Administered every 3 months. - Thicken cervical mucous. - Known to ↓ bone mineral density; rebounds with discontinuation. - Known to cause erratic bleeding in 1/3, no changes in cycle bleeding in 1/3, and complete amenorrhea is 1/3.

	- The answer on 2CK form for woman who normally forgets to take contraception + needs something more reliable + <i>has had STI within the past 3 months</i> . This is because IUD is contraindicated if STI within past 3 months.
Implantable rod	- Aka Implanon/Nexplanon. - Releases progesterone analogue; thickens cervical mucous; lasts 3 years.
Diaphragm	- Cervical cap that covers the uterus; often inserted with spermicidal jelly. - Prevents sperm from entering uterine cavity.



Abortion	
Plan B	- Emergency contraceptive meds. - Levonorgestrel (progesterone analogue); effective within 3 days. - Ulipristal (selective-progesterone receptor modulator; SPRM); effective within 5 days. - Once again, copper IUD can be used for emergency contraception and is most effective if inserted.
Plan C	- Abortion meds. - Mifepristone (progesterone receptor antagonist) is used up to 10 weeks post-intercourse. - This is followed by misoprostol (PGE1 analogue) 1-2 days later.
Plan D	- Surgical abortion. - Vacuum aspiration can be done 6-16 weeks. - Dilation and evacuation (D&E) done >16 weeks.



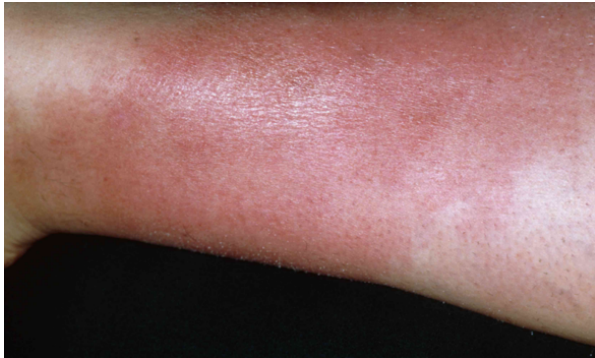
Hormone replacement therapy (HRT)
<ul style="list-style-type: none"> - Estrogen combined with progesterone; only approved for severe perimenopausal vasomotor symptoms (i.e., hot flashes, urge incontinence, atrophic vaginitis). - Not given to help preserve bone density or for positive role on mood and neurocognition, since ↑ absolute estrogen exposure in women ↑ risk of breast cancer, MI, and thromboembolic events (i.e., DVT, PE, stroke). The latter is because estrogen upregulates fibrinogen and factors V and VIII. - Can cause unopposed estrogen and ↑ endometrial cancer risk only if the woman inadvertently stops taking the progesterone component (i.e., endometrial hyperplasia → ↑ endometrial adenocarcinoma risk). - Estrogen alone can be considered only if the woman has Hx of hysterectomy (i.e., no ↑ endometrial adenocarcinoma risk). - Can cause ↓ libido due to ↓ endogenous androgen production (i.e., ↑ negative-feedback at hypothalamus / anterior pituitary → ↓ GnRH → ↓ LH and FSH).



Repro/obgyn drugs	
- Not meant to be exhaustive list; just HY ones for IM.	
Aromatase inhibitors	<ul style="list-style-type: none"> - ↓ Conversion of androgens to estrogens. - Letrozole is used to stimulate ovulation by ↓ negative-feedback at hypothalamus / anterior pituitary. Some students ask about this agent in comparison to clomiphene (discussed below). The literature seems to be split on it, and I haven't seen NBME give a fuck. - Anastrozole and exemestane are used for breast cancer in post-menopausal women.
BPH meds	<ul style="list-style-type: none"> - Finasteride is 5α reductase inhibitor used for BPH. ↓ conversion of testosterone to DHT. Since DHT causes prostatic growth, ↓ DHT means ↓ prostatic growth. - Tamsulosin/terazosin are α1 blockers that ↓ constriction of internal urethral sphincter of the bladder and help promote urinary outflow.
Clomiphene	- Selective-estrogen receptor modulator (SERM) used to stimulate ovulation in those with irregular cycles (in particular those PCOS).




	<ul style="list-style-type: none"> - Has partial-agonist effects at the hypothalamus that are weaker than endogenous estrogen, so the hypothalamus interprets this as ↓ estrogen is present, so negative-feedback also ↓ → GnRH ↑.
Danazol	<ul style="list-style-type: none"> - Androgen-receptor partial agonist. - Theoretically a med that can be used for endometriosis, but USMLE doesn't assess this use-case. - Used for hereditary angioedema, where it stimulates the liver to synthesize more C1-esterase inhibitor. - Can cause hirsutism and pseudotumor cerebri.
GnRH receptor agonists	<ul style="list-style-type: none"> - Leuprolide, goserelin, and nafarelin are all GnRH receptor agonists. When administered continuously, they cause desensitization of the GnRH receptor at the anterior pituitary, leading to ↓ LH and FSH secretion (i.e., even though the drugs are pharmacologic agonists, they function clinically as antagonists).
HTN meds	<ul style="list-style-type: none"> - Methyldopa (α_2 receptor agonist), labetalol, and nifedipine classically used. - Hydralazine used for HTN emergencies in pregnancy.
Magnesium	<ul style="list-style-type: none"> - Used in severe preeclampsia to prevent seizures (eclampsia). - Used to treat seizures in eclampsia. - Given to women giving birth <32 weeks' gestation as a neuroprotective agent for the neonate. - Can in theory be used as tocolytic (discussed below).
Methotrexate	<ul style="list-style-type: none"> - Given for small, stable ectopic pregnancies – i.e., mother is hemodynamically stable, there is no evidence of tubal rupture / fluid in the peritoneal cavity, the ectopic is <3.5 cm, and β-hCG is <5000 mIU/mL.
Minoxidil	<ul style="list-style-type: none"> - Arteriolar dilator that promotes hair growth in androgenetic alopecia. - USMLE wants you to know the latter is polygenic and risk is ↑ with anabolic steroids.
SERMs	<ul style="list-style-type: none"> - SERMs are agents that have different effects depending on the tissue. - Tamoxifen and raloxifene are SERMs used for estrogen-receptor (+) breast cancer, where they both are antagonistic at breast and agonistic at bone. - Tamoxifen causes ↑ risk of endometrial cancer due to agonistic effects at endometrium.
Tocolytics	<ul style="list-style-type: none"> - Suppress labor by ↓ uterine contractions; often utilized to delay premature labor to allow for fetal lung maturity while two boluses of corticosteroids are administered. - Terbutaline (mixed $\beta_1/2$ agonist), ritodrine (β_2 agonist), and nifedipine are HY ones. - Indomethacin and magnesium can also technically be used for this reason.



IM Derm




HY Derm conditions for IM	
Tinea capitis	 <ul style="list-style-type: none"> - Cause is dermatophytes (i.e., <i>Microsporum</i>; <i>Trichophyton</i>). - Classically circular, scaly area of scaly alopecia. - Tx = oral griseofulvin for patient only; “patient + classmates” is wrong answer on NBME. - Another NBME Q asks how to prevent; answer = “avoidance of sharing of hats”; “use of medicated shampoo” is wrong answer.
Seborrheic dermatitis	 <ul style="list-style-type: none"> - Inflammatory response to over-colonization with <i>Malassezia</i> yeast. - Presents as itchy scalp with flakes. If severe, presents as “weeping papules” / scaling of the hairline. - More common in adults. - Don’t confuse with tinea capitis above, which is a circular area of scaling alopecia more common in children. - Tx = Topical selenium or ketoconazole shampoo;; cause. - Can sometimes occur in HIV patients; sudden onset in high-risk group → answer = do HIV test.
Tinea corporis	<ul style="list-style-type: none"> - Aka ringworm. - Q will often mention a dog at home. - Tx = topical miconazole or clotrimazole. - Tx for tinea pedis (athlete’s foot) is topical terbinafine or topical -azole.



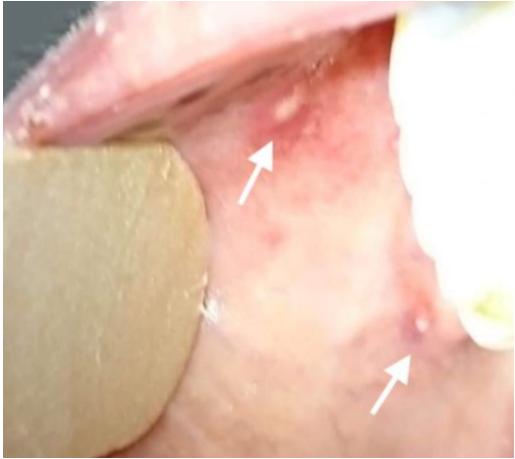
	
Lymphangitis	 <ul style="list-style-type: none"> - Above image shows sporotrichosis (<i>Sporothrix schenckii</i>), but similar pattern can also be seen for miscellaneous burns or puncture wounds of the hand that cause ascending infection toward the axilla. - Students early in their prep know that <i>Sporothrix</i> is classically a papule on the finger caused by rose thorns; this presentation is usually too easy for real USMLE though. - Treatment for sporotrichosis is oral itraconazole. - USMLE can show image similar to the above, where they list answers like phlebitis, arteritis, lymphangitis, etc.; answer is just "lymphangitis."
Cellulitis	 <ul style="list-style-type: none"> - <i>Staph aureus</i> exceeds <i>Strep pyogenes</i> (Group A Strep) as causal organism; must give beta-lactamase-resistant beta-lactam in the methicillin class (i.e., dicloxacillin, flucloxacillin) or first-generation cephalosporin (i.e., cephalexin, cephalazolin), or Augmentin (amoxicillin-clavulanate). - Amoxicillin and penicillin alone are wrong answers.




	<p>- 90% of community <i>Staph</i> (i.e., MSSA) produces beta-lactamase, so amoxicillin and penicillin alone will not work if <i>Staph</i> is the cause.</p>
Erysipelas	 <ul style="list-style-type: none"> - Infection of upper dermis and superficial lymphatics. - Caused by <i>Strep pyogenes</i> (Group A Strep), which eclipses <i>Staph aureus</i> for erysipelas. - Looks worse than cellulitis but is more superficial / “not as bad”; has characteristic “fiery red” appearance and may appear well-demarcated with raised edges. - Although Group A Strep > <i>Staph</i> for erysipelas, Tx is same as cellulitis (oral dicloxacillin, cephalexin, or Augmentin) because <i>Staph</i> can still cause it. Penicillin alone can be used for <i>Strep</i> pharyngitis.
Acne	 <ul style="list-style-type: none"> - Caused by <i>Propionibacterium acnes</i>; not difficult, but I’ve seen enough students select tinea faciei (fungal infection of face) for simple acne. - First-line Tx for acne on USMLE is topical retinoids (i.e., topical tretinoin; not oral isotretinoin; latter is only for severe acne). Topical retinoids (vitamin A) inhibit sebum production; they cause photosensitivity and desquamation (peeling). - Topical benzoyl peroxide is second-line for acne (although often co-administered with topical tretinoin). It clears pores and kills bacteria. - Topical clindamycin can be used if topical retinoids and benzoyl peroxide are insufficient; if topical antibiotic is insufficient, oral tetracycline is used; the latter causes blistering photosensitivity. - Last resort is oral isotretinoin; must do beta-hCG (pregnancy test) before commencement due to teratogenicity; oral isotretinoin does not cause problems with sperm in men; topical retinoids in both men and women do not cause teratogenicity.



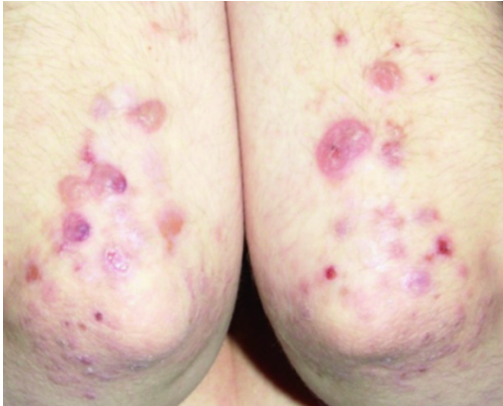
	 <p>- Above image shows the HY photosensitivity due to topical retinoids; answer = “avoidance of sun exposure”; tetracycline photosensitivity, in contrast, tends to be blistering; do not choose answers such as “avoidance of spicy/sweet foods” for acne questions.</p>
Tinea faciei	 <p>- Fungal infection of face. - Tx = topical -azoles (clotrimazole, miconazole).</p>
Meningococcus	 <p>- <i>Neisseria meningitidis</i>; gram-negative diplococcus. - Causes meningitis + characteristic non-blanching rash. - Low BP can be endotoxic shock, but student should bear in mind Waterhouse-Friderichsen syndrome is often asked; give hydrocortisone to increase BP after normal saline is administered.</p>




<p>Herpetic whitlow</p>	 <ul style="list-style-type: none"> - One of the highest-yield spot-diagnoses on USMLE. - HSV1/2 infection of the finger. - In children, can be acquired via touching mother's cold sore (e.g., during breastfeeding). - In adults, classically dental workers. - Tx = topical and oral acyclovir.
<p>Lyme disease</p>	 <ul style="list-style-type: none"> - <i>Borellia burgdorferi</i>; a spirochete. - Spirochete; spiral/corkscrew-shaped. - Causes Lyme disease; spread by <i>Ixodes</i> tick (same as <i>Ehrlichia</i>, <i>Babesia</i>, and <i>Anaplasma</i>). - Primary Lyme causes a classic target rash known as erythema chronicum migrans, but a HY point is that the rash need not be a target on USMLE. It can merely be circular with no clearing, but the target is classic. - Bells palsy can also be seen in primary Lyme. What the USMLE will do is give two side by side images: 1) circular rash on limb that is not a target; 2) Bells palsy, where the student needs to infer this is Lyme disease even though rash isn't a target, since Bells palsy is HY for Lyme. - Secondary Lyme tends to cause arthritis. Some sources say Bell's palsy is part of secondary Lyme (occurs at least one month after initial infection), but I've seen USMLE give it as part of initial/primary infection. - Tertiary Lyme can cause CNS and/or heart problems. - Treatment is doxycycline for most cases of Lyme. - Ceftriaxone is given for advanced Lyme involving the CNS or heart. - For children <8 and pregnant women, give amoxicillin in place of doxycycline. - There is an NBME Q of a pregnant woman with non-disseminated Lyme, where ceftriaxone is correct over doxycycline, and amoxicillin isn't listed. In other words, if




	<p>USMLE doesn't want doxy as the answer, they will not play trivia as to whether it's ceftriaxone or amoxicillin to be used as the alternative. But you could be aware that, in theory, ceftriaxone is harder-hitting and preferred if cases are more severe.</p>
Scabies	 <ul style="list-style-type: none"> - <i>Sarcoptes scabiei</i>. - Lesions classically described as "linear burrows". - Can become superinfected with <i>Staph aureus</i>. - Tx = topical permethrin. - Disseminated scabies can occur in HIV patients; Tx is oral ivermectin. - Topical permethrin is also treatment for pediculosis (lice).
Bed bugs	 <ul style="list-style-type: none"> - Caused by an insect called <i>Cimex</i>. - Grows as clusters of itchy lesions on the limbs or torso.
Cutaneous anthrax	 <ul style="list-style-type: none"> - Caused by <i>Bacillus anthracis</i>. - Classically causes a black "eschar." - Seen in postal workers + farmers. - Pulmonary anthrax leads to hemorrhagic mediastinitis. - Tx = ciprofloxacin.

Tularemia	 <ul style="list-style-type: none"> - Caused by <i>Francisella tularensis</i>. - cutaneous tularemia can present as ulcerative lesions; can also cause bilateral atypical pneumonia; rabbits are classic source. - Tx = doxycycline.
Hot tub folliculitis	 <ul style="list-style-type: none"> - Rash caused by <i>Pseudomonas</i> from water sources. - Increased risk in diabetics.
Measles	 <ul style="list-style-type: none"> - Aka rubeola; causes a head-to-toe macular popular rash. - Image shows Koplik spots (pathognomonic whiteish lesions on buccal mucosa). - Immigrant Hx on USMLE sometimes implies unvaccinated status. - Can rarely cause subacute sclerosing panencephalitis (reactivation of latent infection in the CNS in teenagers).




	<ul style="list-style-type: none"> - Rubella also causes a head-to-toe macular popular rash, but rather than Koplik spots, suboccipital and post-auricular lymphadenopathy (tenderness on back of head and behind ears) is characteristic.
Mumps	 <ul style="list-style-type: none"> - Causes POM → Parotitis, Orchitis, Meningitis. - Doesn't typically cause rash.
Parvovirus B19	 <ul style="list-style-type: none"> - Fifth disease = "slapped cheek" facial erythema caused by Parvo B19 in Peds. - Next best step = check serum IgM titers; if IgM titers are not listed, choose bone marrow biopsy. - Can cause pure-RBC aplasia (i.e., only RBCs are low) or full-blown aplastic anemia (where all cell lines - RBCs, WBCs, and platelets - are down). There is increased risk of pure-RBC aplasia and aplastic anemia in sickle cell. - Once child has developed the red cheeks, he/she has immunologically cleared the illness (i.e., if they turn it into a behavioral science Q, tell parents to chill the fuck out / relax because the child has cleared the virus).  <ul style="list-style-type: none"> - Can cause body rash +/- arthritis in adults; same as with Fifth disease, next best step is check serum IgM titers.




Roseola	 <p>- Caused by HHV6; described as “spiking fever followed by a rash” – i.e., child will have high fever for 2-3 days, followed by a rash.</p>
Eczema herpeticum	 <p>- HSV1/2 infection superimposed on eczema. - Often self-inoculated from touching cold sore then cracked skin of eczema. - Herpes infection can present with fever, lymphadenopathy, and tingling, burning, and painful rash (herpetic neuralgia). - Tx = acyclovir.</p>
Dermatitis herpetiformis	 <p>- Extra-intestinal cutaneous eruption that can occur in patients with Celiac disease. - Despite the name, this is not actual herpes. It is IgA deposition at dermal papillae. - Don't confuse with eczema herpeticum.</p>


Hidradenitis suppurativa	<ul style="list-style-type: none"> - Skin condition characterized by painful abscesses and sinus tracts, most commonly in the groin, axilla, and under the breasts; frequently affects apocrine glands. - Cause is a combination of genetic and environmental factors (idiopathic). - NBME answer is "surgical excision of lesions." 
Pediatric shingles	 <ul style="list-style-type: none"> - You need to know that pediatric shingles "is a thing." - Classically seen in immunocompromised children (e.g., due to chemotherapy). - Shingles is aka "herpes zoster" and is caused by varicella zoster virus (VZV); herpes zoster is not a virus name; herpes zoster literally is just another name for shingles, which is caused by VZV (human herpes virus 3; HHV3), not HSV1/2 (HHV1/2).
Herpes zoster oticus	 <ul style="list-style-type: none"> - VZV (shingles) causing periaural lesions. - Can concurrently affect CN VII leading to Bells palsy (Ramsay-Hunt syndrome II).
Kaposi sarcoma	




	 <ul style="list-style-type: none"> - Caused by HHV 8 (Kaposi sarcoma-associated herpes virus) in immunocompromised patients (i.e., AIDS, chemotherapy). - Kaposi sarcoma are violaceous, tumorous lesions of vascular-lymphatic origin. - Q can show you image such as above and then the answer is just “anti-neoplastic” for the Tx (whereas answers like anti-fungal, anti-bacterial, etc., are wrong).
Pityriasis rosea	 <ul style="list-style-type: none"> - Caused by HHV6 or 7; self-limiting. - Starts as Herald patch (larger pink ellipse above), usually on the back or trunk, then spreads upward onto the shoulder blades (“Christmas tree distribution”); USMLE will show you image and expect you can make spot-diagnosis. - Can occur in teenagers, although more common in the 20s.
Tinea versicolor	 <ul style="list-style-type: none"> - Caused by <i>Malassezia furfur</i>; fungus causes spotty hypopigmentation; patient usually lives in sub-tropical areas like Florida. - Can occur in teenagers who surf / go to the beach. - Tx = topical selenium.




<p>Molluscum contagiosum</p>	 <ul style="list-style-type: none">- Very HY spot-diagnosis for Peds; caused by Poxvirus.- Classically skin-colored or reddish papules with central umbilication.- USMLE likes giving vignette where kid went to a recent pool party.
<p><i>Mycobacterium marinum</i></p>	 <ul style="list-style-type: none">- Unusual diagnosis but asked.- Vignette will say kid recently went to aquarium or water park + now has red lesions on the hand/arm.- Can occur in adults as well who work at aquariums or water parks.
<p>Leishmaniasis</p>	 <ul style="list-style-type: none">- <i>Leishmania donovani</i>; protozoan; unicellular eukaryote; spread by sandfly bite.




	<ul style="list-style-type: none"> - Can cause skin ulcer; USMLE likes Middle East as endemic (I've seen Iraq on NBME). - Visceral disease known as kala azar, which causes ↑ LFTs and pancytopenia.
MAI	 <p>- <i>Mycobacterium avium intracellulare</i> (MAI); can cause lymphadenitis with classic reddish/violaceous lesion on the neck or pre-auricularly.</p>
Secondary syphilis	 <ul style="list-style-type: none"> - <i>Treponema pallidum</i> (spirochete); image shows maculopapular/nodular body rash; palms and soles are classically affected in 2ndary syphilis but Q need not mention it. - Diagnosed with serology; VDRL/RPR ordered before FTA, but latter more specific. - VDRL can be falsely positive in patients with antiphospholipid syndrome (usually SLE patients with lupus anticoagulant). - USMLE Q can also show you picture of condylomata lata (wart-like lesions on the genitals) + tell you there's palms/soles rash, then answer = <i>Treponema pallidum</i>. Tx = penicillin.
Arsenic poisoning	




	<ul style="list-style-type: none"> - Mees lines are white lines seen on fingernails in arsenic toxicity. - Arsenic is present in small amounts in fertilizers, which causes plants to flourish; gardeners at increased risk. - Arsenic can also cause palms/soles rash (arsenical keratosis).
Eczema	 <ul style="list-style-type: none"> - Type I (immediate); can occur as part of atopy (i.e., asthma in winter, hay fever / rhinoconjunctivitis in spring; eczema in summer). - Remember that 1/3 of asthma patients have cough-variant asthma (i.e., only have dry cough, usually worse in the winter or with exercise). - Treat with oil-based emollient and topical corticosteroids; if steroids used >5-7 days continuously, thinning of the dermis may occur.
Urticaria	 <ul style="list-style-type: none"> - Aka hives; type I hypersensitivity; can be precipitated by various allergens, including pollen, pet dander, and drugs.
Erythema multiforme	




	<ul style="list-style-type: none"> - Immune complex-mediated rash (type III hypersensitivity) with many etiologies; HSV1/2 infection is classic cause.
Erythema nodosum	 <ul style="list-style-type: none"> - Panniculitis (inflammation of subcutaneous fat) that resembles a rash. - Seen with autoimmune diseases like sarcoidosis and Crohn, as well as part of serum sickness due to medications (e.g., sulfa).
Dermatomyositis	 <ul style="list-style-type: none"> - Image shows heliotrope rash (left) and shawl rash (right) seen in dermatomyositis. - Anti-Jo1 antibodies and electromyography + nerve conduction studies = diagnostic. - Do not confuse heliotrope rash of dermatomyositis with malar rash of SLE. - Give steroids for flares.  <ul style="list-style-type: none"> - Patients can also get Gottron papules (above image) and “mechanics’ hands” (i.e., rough-surfaced / scaly hands).




Vitiligo	 <ul style="list-style-type: none"> - T cell-mediated destruction of melanocytes. - Relevance for IM is that it can be associated with other autoimmune polyglandular syndromes, as well as IgA deficiency. - For example, B12 deficiency + vitiligo = possible pernicious anemia; or weight gain and fatigue + vitiligo = possible Hashimoto. Etc.
Lentigo	<ul style="list-style-type: none"> - "Age spot." - ↑ melanocyte #; no change melanin production. - Common on zygoma due to sunlight; not malignant. 
Latex allergy	 <ul style="list-style-type: none"> - Q will give you a nurse or laboratory technician. The implication is that he/she has been using gloves resulting in contact dermatitis due to latex. - Can also occur due to adhesives (i.e., from bandages applied).

Rosacea	 <ul style="list-style-type: none"> - Idiopathic patchy facial erythema that worsens with spicy foods and alcohol; slight pain of rash may occur in cold weather. - Occurs usually in middle-age and older.
Chilblains	 <ul style="list-style-type: none"> - Aka perniosis; painful inflammation of distal capillaries due to repeated exposure to cold air, followed by immersion in hot water (i.e., from bath/shower). - This is different from frostnip and frostbite. Frostnip is cold-exposed skin (effects quickly reversible; no skin damage); frostbite is more severe and can result in damage such as blistering and necrosis. - Chilblains can be confused with tinea pedis, since they can be extremely itchy. The patient might self-attempt topical antifungal sprays/foams to no avail. - Tx = keep feet warm in winter; avoid abrupt temperature changes.
Aphthous ulcer	 <ul style="list-style-type: none"> - Aka aphthous stomatitis; no Tx necessary; not related to HSV1/2; etiology is multifactorial; can be precipitated by allergens such as spice; T cell-mediated.



Lichen planus	 <p>- Classically described as “The Ps” → purple, pruritic, polygonal papules; however Qs need not mention they’re pruritic; you just need to know hepatitis C + red/purple skin lesions = lichen planus.</p>
Aplasia cutis congenita	 <p>- Absence of skin on an area of scalp; can be caused by teratogens such as methimazole; dumb/seemingly pedantic detail, I know, but it shows up on real deal.</p>
Hereditary angioedema	 <p>- Deficiency of C1 esterase <i>inhibitor</i> (not C1 esterase alone). - Characterized by recurrent swelling of various bodily regions. - Tx = Danazol (androgen receptor partial agonist causes liver to produce more C1 esterase inhibitor).</p>




NF1	 <ul style="list-style-type: none"> - Neurofibromatosis type I; autosomal dominant; one of the phakomatoses (neurocutaneous disorders → NF1/2, VHL, TSC, Sturge-Weber). - Image shows café au lait spot. - NF1 → café au lait spots, neurofibromas, axillary/groin freckling, optic glioma, pheochromocytoma.
Tuberous sclerosis	<ul style="list-style-type: none"> - Autosomal dominant; one of the phakomatoses. - Image shows adenoma sebaceum (angiofibromas). - Intracranial/periventricular nodules ("tubers" – i.e., hamartomas), adenoma sebaceum (angiofibromas), cardiac rhabdomyoma, lymphangioleiomyomatosis, subungual fibromas, renal angiomyolipoma.  <p>Image shows adenoma sebaceum</p>
Sturge-Weber	 <ul style="list-style-type: none"> - Classically Port Wine-stain birthmark (nevus flammeus), but can be described as "violaceous papules in a temporal distribution." - Associated with leptomeningeal angioma (causing seizure) and glaucoma. - Condition is not inherited and is due to somatic mosaicism.




<p>McCune-Albright syndrome</p>	 <p>- Triad of “coast of Maine” café au lait spots (above image), polyostotic fibrous dysplasia (bone is replaced by fibrous tissue), and endocrine hypersecretion (classically precocious puberty).</p>
<p>Acanthosis nigricans</p>	 <p>- Brown/black velvety skin, usually along nape of neck. - Associated with hyperinsulinemia and type II diabetes almost always. - Can also very rarely be seen in patients with underlying, visceral malignancy.</p>
<p>Basal cell carcinoma (BCC)</p>	 <p>- Classically pearly / slightly translucent; telangiectasias common; borders can sometimes be described as “heaped up” or “rolled”; may or may not be ulcerated. - Treatment for skin cancers on cosmetically sensitive areas such as the eyelid or nose can be managed with Mohs micrographic surgery (on NBME).</p>




Actinic keratoses	 <p>- Aka solar keratoses; precursor to squamous cell carcinoma (SCC); classically described as red/scaly lesions on forehead, ear, or arms of fisherman, farmers, or construction workers. Cryotherapy is usual treatment.</p>
Squamous cell carcinoma (SCC)	<p>- Ulcerated lesion in the setting of a patient who's had actinic keratoses – i.e., Q says patient has had scaly red areas on forehead for many years + now has recent ulceration → answer = SCC.</p> <p>- SCC will not have telangiectasias or pearly/translucency (as with BCC).</p> 
Keratoacanthoma	 <p>- Can be confused with SCC; described as dome-shaped with a hyperkeratotic core, surrounded by a wall of inflamed skin.</p> <p>- Tx is surgical excision.</p>



<p>Melanoma</p>	<div data-bbox="667 226 1171 624" data-label="Image"> </div> <ul style="list-style-type: none"> - Depth is most important for prognosis. - Answer on NBME = excisional biopsy; suspected malignant lesions in non-cosmetically sensitive areas (i.e., not on the head/neck) can simply be excised with narrow margins; excision of additional tissue is important if margins are positive (i.e., entire lesion wasn't excised). - "Full-thickness biopsy" answer on USMLE for suspected melanoma on back of neck (NBME Q gives lesion similar to above on neck, with full-thickness biopsy as answer). Excision of lesion is management for neck lesions if full-thickness biopsy confirms melanoma; do Mohs micrographic surgery for facial lesions. - Punch biopsy is a type of full-thickness biopsy; if Q asks, choose side of lesion for biopsy, rather than middle of lesion. - Students will sometimes ask about shave biopsy. I have never seen this assessed on NBME, but literature says it can sometimes be used to remove superficial non-pigmented lesions where the clinician does not suspect melanoma (performing shave biopsy on melanoma can create problems for assessing depth, prognosis, and therapy). <div data-bbox="742 1207 1096 1561" data-label="Image"> </div> <ul style="list-style-type: none"> - Acral lentiginous melanoma occurs on the palms/soles (areas not usually exposed to sun); more common in persons of African and Asian descent. <div data-bbox="726 1688 1112 1977" data-label="Image"> </div> <ul style="list-style-type: none"> - Can also occur under the finger nail.
-----------------	---




<p>Seborrheic keratoses</p>	 <ul style="list-style-type: none"> - Sun exposure and old age are biggest risk factors; also seen in smokers. - Described as “greasy,” or waxy, skin growths that appear like they can be “peeled off”; not malignant. - Sign of Leser-Trélat = sudden, eruptive seborrheic keratoses secondary to underlying, visceral malignancy (i.e., unrelated to age or sun).
<p>Blue nevus</p>	<ul style="list-style-type: none"> - Aka Mongolian spot. - Type of benign birthmark where dermal melanocytes fail to migrate superficially to stratum basale. - More common in Asians and blacks. - Often mistaken for child abuse. - Schedule routine follow-up; wrong answer is contacting child protective services. 
<p>Strawberry hemangioma</p>	 <ul style="list-style-type: none"> - Benign capillary tumor that will grow slightly then regress spontaneously within a few years. - No Tx necessary unless causing functional impairment. - Don't confuse with cherry hemangioma, which is due to sun exposure in elderly and presents as a tiny cherry-colored papule.



Cherry hemangioma	 <p>- Benign capillary tumors caused by sunlight; benign; greater prevalence as age ↑. Students confuse with strawberry hemangioma in peds.</p>
Preauricular pit	 <p>- Preauricular pits are benign finding, usually not associated with any congenital disorder. - No Tx necessary. Can become infected; do surgical closure if frequent infections.</p>
Kasabach-Merritt syndrome	 <p>- Aka infantile hemangioma with thrombocytopenia; asked several times on 2CK assessments. - Child will have thrombocytopenia due to platelet sequestration within the lesion. - Large and deforming; don't confuse with strawberry hemangioma. - Tx is surgical.</p>

Cushing syndrome	 <ul style="list-style-type: none">- USMLE wants you to know purple striae are HY physical exam finding.- Weakening of dermal collagen + capillary walls → micro bleeding into skin.
Cigarette burn	 <ul style="list-style-type: none">- Q will show you image similar to above and then the answer will be “contact child protect services”; can also be on face / resemble impetigo if at different stages of healing.
Keloids	<ul style="list-style-type: none">- Disorganized growth of dermal collagen.- Tx is surgical excision, although recurrence is common. Benign. 

<p>Pseudofolliculitis barbae</p>	 <p>- Aka razor bumps; increased prevalence in African descent; curly beard hair grows back into the skin; Tx is to allow the beard to grow; USMLE Q will show you image and just ask the spot-Dx.</p>
<p>Milia</p>	 <p>- Aka "milk spots"; clogged eccrine ducts; common, benign finding in babies. - No Tx necessary; - "Exfoliative cleanser" and "topical low-dose corticosteroid" = wrong answers.</p>
<p>Varicose veins</p>	<p>- Q will ask next best step in diagnosis → answer = duplex venous ultrasonography for venous disease / valvular insufficiency. - Tx is compression stockings. - Do not choose surgical interventions for varicose veins on USMLE.</p> 

<p>Superficial thrombophlebitis</p>	 <ul style="list-style-type: none"> - Similar to DVT, but in more superficial vein; presents as painful, warm, “palpable cord” at the ankle that may or may not track up to the knee. - Treated with subcutaneous enoxaparin (heparin); wrong answer is compression stockings; very difficult Q since compression stockings are common answer for venous disease, but if patient has active venous occlusion (i.e., DVT or superficial thrombophlebitis), give heparin. - In other words, for simple venous disease / varicose veins, choose compression stockings, but if the patient has an active clot presenting as a palpable vein with pain, give heparin instead.
<p>Buerger disease</p>	 <ul style="list-style-type: none"> - Aka thromboangiitis obliterans; condition is digital gangrene in males who are heavy smokers; contrasts with gangrene due to diabetes, which is pedal. - Tx = smoking cessation.
<p>Charcot joint</p>	<ul style="list-style-type: none"> - Aka neurogenic joint; mechanism is “lack of appropriate joint sensation” – i.e., patient can feel his or her feet due to neuropathy → damage → can’t heal the area due to vasculopathy. - Q will be diabetic with poor HbA1c + foot ulcer + x-ray of the shows disorganization of the tarsals/metatarsals.

	
Cryoglobulinemia	<p>- Cryoglobulins are immune complexes that precipitate at cold temperatures.</p>  <p>- Often presents as livedo reticularis, which is a mottled, reticulated vascular pattern that has many etiologies; associated with hepatitis C.</p> <p>- Cryoglobulinemia is associated with decreased serum complement protein C4 (in contrast, C3 is sometimes down in SLE flares and Group A Strep infections).</p>
SVC syndrome	 <p>- Image shows Pemberton sign (facial erythema due to diminished venous return when arms are raised above head).</p> <p>- Seen classically in Pancoast (i.e., apical) tumors of the lung.</p>

<p>Actinic purpura</p>	 <ul style="list-style-type: none">- Aka senile or solar purpura.- Flat, purple discolorations caused by damage to dermal collagen and blood vessels due to chronic sun exposure.- Commonly appear on the back of the hands and forearms in elderly.- Benign; may be mistaken for bruises.- NBME Q describes actinic purpura and then asks for mechanism. The answer is "solar elastosis," which is a term that refers to degenerative changes to the dermis due to chronic sun exposure.
<p>Keratosis pilaris</p>	<ul style="list-style-type: none">- Benign bumps + rough patches on the skin due to build-up of excess keratin.- The excess Keratin can block hair follicles and pores, causing small, hard bumps.- No treatment necessary. Emollients may be used.- Not obscure condition I'm mentioning for fun. Shows up on NBME. 

IM Neuro

Stroke risk factors
<ul style="list-style-type: none"> - The two most important risk factors for stroke (cerebral infarction) on USMLE are hypertension and atrial fibrillation. - Regarding HTN, a strong systolic impulse pounds the carotid arteries, leading to endothelial damage and increased development of atherosclerotic plaques (carotid stenosis), which then launch off to the brain/eye. - Atrial fibrillation results in turbulence and stasis, leading to left atrial mural thrombus, which launches off. - Hypertension is most common in the population for causing stroke. Blood pressure control is more important than smoking cessation for decreasing stroke risk. - If the USMLE Q gives you a patient who has both AF and HTN, they want AF as the most important risk factor. In other words, even though HTN is the most common risk factor in the population for stroke, AF is still more likely to cause stroke if the patient has both. - There are other details regarding stroke I will discuss in this PDF, but for starters, these risk factors are pass-level points for understanding how/why most strokes occur – i.e., “How do most strokes occur?” → “Oh, well the patient will usually have carotid stenosis from HTN, where an atheromatous plaque has launched off, or will have AF where an LA mural thrombus has launched off.” Simple. - I discuss carotid stenosis and AF management for stroke prevention in detail in the HY Cardio PDF.

Circle of Willis HY strokes	
Affected vessel	HY Points
ACA	<ul style="list-style-type: none"> - Anterior cerebral artery. - Motor/sensory abnormalities of contralateral leg.
MCA	<ul style="list-style-type: none"> - Middle cerebral artery. - Motor/sensory abnormalities of contralateral arm + face. - Dominant MCA stroke (usually left) can lead to Wernicke or Broca aphasia (discussed below). - Non-dominant MCA stroke (usually right) can cause hemispatial neglect (inability to draw clockface).
PCA	<ul style="list-style-type: none"> - Posterior cerebral artery. - Contralateral homonymous hemianopsia with macular sparing. - Prosopagnosia (inability to recognize faces).

Other stroke syndromes	
Lateral medullary syndrome	<ul style="list-style-type: none"> - Aka Wallenberg syndrome. - The answer for dysphagia + ipsilateral Horner syndrome after a stroke. - Due to stroke of posterior inferior cerebellar artery (PICA) or vertebral artery. - PICAchew (Pikachu) → PICA stroke causes dysphagia. - Students might know Horner syndrome (ipsilateral miosis, partial ptosis, anhidrosis) can be caused by Pancoast tumor, but another HY cause is lateral medullary syndrome.
Medial medullary syndrome	<ul style="list-style-type: none"> - The answer for ipsilateral tongue deviation after a stroke. - Due to stroke of anterior spinal artery.
Lateral pontine syndrome	<ul style="list-style-type: none"> - The answer for ipsilateral Bells palsy after a stroke. - Due to stroke of anterior inferior cerebellar artery (AICA). - FACIAL (contains AICA backwards) → “That’s the one that’s Bells palsy.”
Weber syndrome	<ul style="list-style-type: none"> - Midbrain stroke. - The answer for ipsilateral CN III palsy (i.e., down and out eye) + contralateral spastic hemiparesis (weakness).
Locked-in syndrome	<ul style="list-style-type: none"> - Basilar artery stroke. - The answer for inability to move entire body except for eyes.

Gerstmann syndrome	<ul style="list-style-type: none"> - Stroke of angular gyrus of parietal lobe. - Tetrad of 1) agraphia (inability to write); 2) acalculia (cannot do math); 3) finger agnosia (can't identify fingers); 4) left-right disassociation (cannot differentiate between left and right sides of body).
Hemiballismus	<ul style="list-style-type: none"> - Stroke of subthalamic nucleus. - Causes "ballistic" flailing of contralateral arm and/or leg. - Weird condition, but for some reason asked. For example, if they say patient has random flailing of left arm following a stroke, answer = right subthalamic nucleus.

Lenticulostriate strokes	
Lacunar infarcts	<ul style="list-style-type: none"> - HTN can cause lipohyalinosis (fancy word for microatheroma formation) of small lenticulostriate arteries deep within the brain. - Ischemia within these small vessels leads to necrosis and reabsorption of tissue, leading to tiny cavities called lacunae. - Unlike larger strokes, lacunar infarcts often do not present with cortical deficits like aphasia, neglect, or visual field losses. Instead, they manifest as specific syndromes based on their location, such as pure motor hemiparesis, pure sensory stroke, ataxic hemiparesis. The USMLE doesn't give a fuck about the specific types of lacunar deficits/strokes. They just want you to know they exist / are possible, and that the mechanism is HTN causing lipohyalinosis of these small, penetrating vessels, as mentioned above.
Charcot-Bouchard microaneurysms	<ul style="list-style-type: none"> - Charcot-Bouchard microaneurysms are tiny (<1mm) aneurysms that can form within lenticulostriate arteries that can bleed and cause hemorrhagic strokes / intraparenchymal (intracerebral) bleeds.

HY Aphasia types	
Wernicke	<ul style="list-style-type: none"> - Fluent aphasia (i.e., patient can speak with normal pace + use lots of words), but none of it makes sense ("word salad"). - Ability to comprehend is similarly impaired (i.e., patient makes no sense in terms of what comes out + inability to make any sense of what comes in). - Repetition is impaired (i.e., patient cannot repeat back a sentence spoken to him/her). - Wernicke area is located in the temporal lobe; caused by L-sided MCA infarct.
Broca	<ul style="list-style-type: none"> - Non-fluent aphasia (i.e., patient has "telegraphic speech"), where there is frustration in not being able to communicate despite comprehending normally, akin to trying to communicate in a second language. - Repetition impaired. - Broca area is located in frontal lobe; caused by L-sided MCA infarct.
Conductive	<ul style="list-style-type: none"> - Patient only has repetition impaired. - Stroke of arcuate fasciculus, which is bundle of nerve fibers that connects Wernicke and Broca areas.
Global	<ul style="list-style-type: none"> - Presentation akin to having Broca and Wernicke aphasia at the same time, in addition to repetition being impaired. - Stroke of Broca + Wernicke areas + arcuate fasciculus.
Transcortical sensory	<ul style="list-style-type: none"> - Presentation same as Wernicke but repetition intact.
Transcortical motor	<ul style="list-style-type: none"> - Presentation same as Broca, but repetition intact.

Stroke management / Tx	
Ischemic stroke	<ul style="list-style-type: none"> - Non-contrast CT of the head is done to look for ischemic vs hemorrhagic stroke. If blood is present, it will appear as bright (hyperdense) areas on CT. - If stroke is ischemic (i.e., no blood seen on non-contrast CT), tPA is given if symptom onset has been within the past 4.5 hours and there are no overt contraindications to tPA (discussed below). - The start of the 4.5-hour window refers to when the patient was last confirmed/observed to be normal. So if the patient was sleeping prior to the stroke, it must be known exactly when the patient started sleeping, and if he/she was normal prior to going to bed. - The USMLE can be tricky about this point, where they might say a guy awoke this morning from sleep 2 hours ago + has facial drooping, where tPA is wrong because the stroke could have occurred at any point while he was asleep + the last time he was observed to have no stroke signs was the night before. - If the 4.5-hour window has elapsed, aspirin is the answer for ischemic stroke. - BP should be brought down rapidly until below 185/110 so that tPA can be given. Below this threshold, cautious/slower BP control should be done, since \uparrow BP can actually facilitate perfusion of penumbic areas of ischemia (i.e., areas of ischemia around the stroke).
Hemorrhagic stroke	<ul style="list-style-type: none"> - Do not give tPA. First step is lowering BP (labetalol, nicardipine, or hydralazine). - Reduce BP rapidly to systolic <140 mm Hg. - Reverse anticoagulation if the patient is on it (i.e., FFP for patients on warfarin).

Sodium correction	
Cerebral edema	<ul style="list-style-type: none"> - Correction of hypernatremia too quickly with hypotonic saline can cause cerebral edema.
Central pontine myelinolysis	<ul style="list-style-type: none"> - Correcting hyponatremia too quickly with hypertonic saline causes central pontine myelinolysis. - Can be described as "osmotic demyelination." - Causes locked-in syndrome. <div data-bbox="699 1207 1107 1697" data-label="Image"> </div> <ul style="list-style-type: none"> - USMLE can show MRI of the pons similar to the above.

Hypercalcemic crisis
<ul style="list-style-type: none"> - Refers to cognitive dysfunction / a delirium-like state in the setting of severe hypercalcemia, often due to malignancy or primary hyperparathyroidism. - USMLE wants you to know that high calcium, as well as any sodium disturbance, can cause delirium. - First step on USMLE for Tx of hypercalcemia is normal saline.

- After normal saline, USMLE wants bisphosphonate therapy (I've seen pamidronate listed on NBME).
- I've never seen calcitonin or loop diuretics as correct answers for hypercalcemia Tx. They're always wrong.

Pseudotumor cerebri

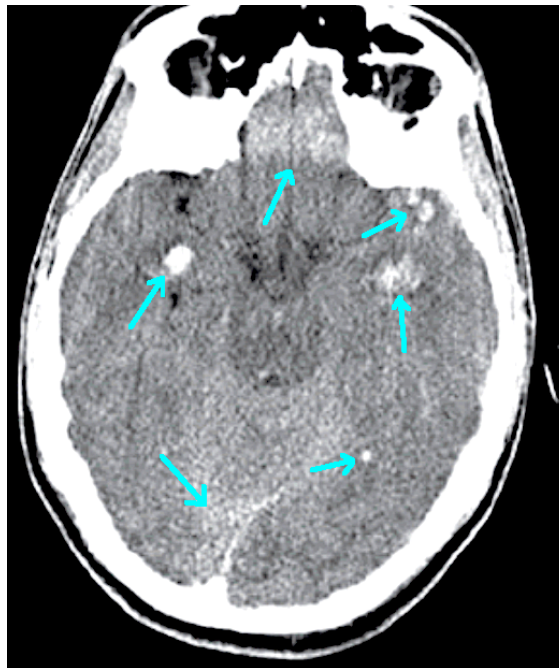
- Term that refers to increased intracranial pressure in the setting of no clear structural cause.
- Some notable causes are obesity (idiopathic intracranial hypertension), OCPs, isotretinoin, and danazol.

Reye syndrome

- Cerebral edema and hepatotoxicity seen with administration of aspirin to children (and sometimes adolescents) during a viral infection.
- Thought to be due to impairment of beta-oxidation, but USMLE doesn't care.

Diffuse axonal injury

- Deceleration injury (e.g., car accident) followed by severe cognitive and/or motor/sensory dysfunction (i.e., following an MVA, the patient has to relearn tying his/her shoes, etc.).
- USMLE can show MRI showing scattered hyperintense (white) lesions.

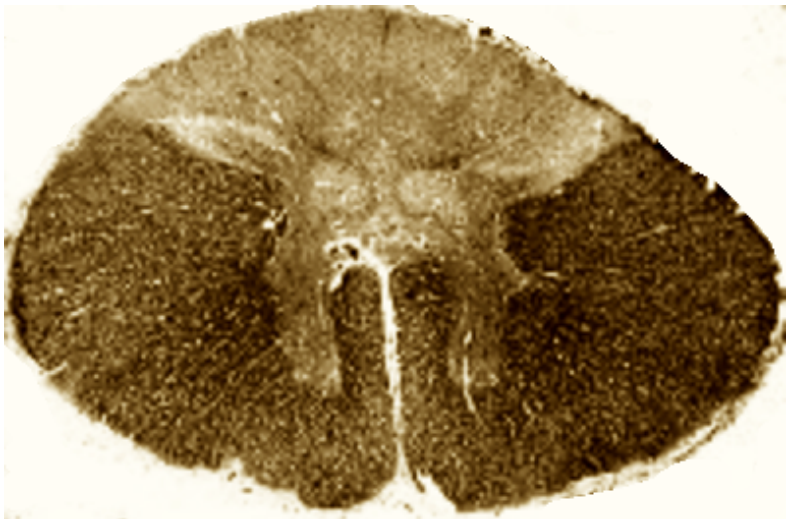


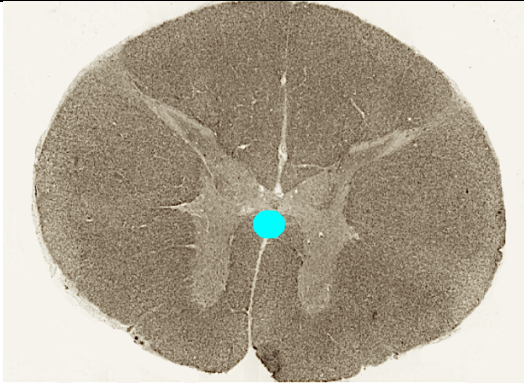
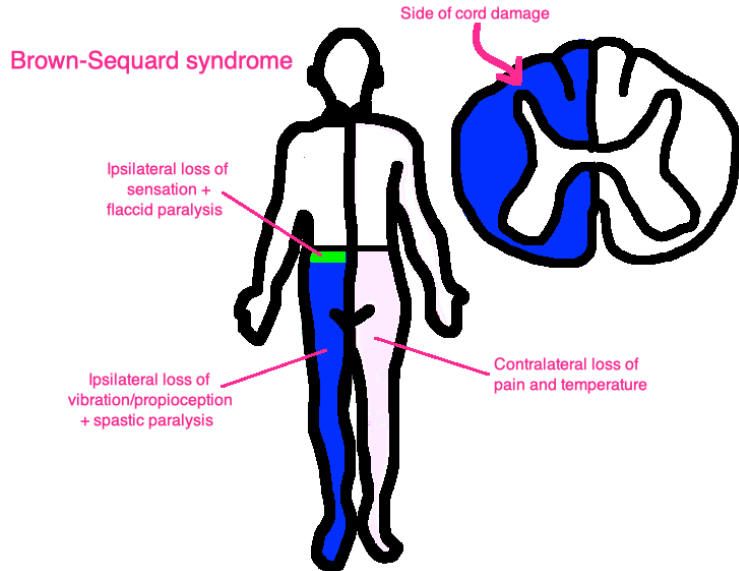
Pass-level spinal tract functions



Spinothalamic tract	<ul style="list-style-type: none"> - Pain and temperature sensation from contralateral body. - Cross-over (decussation) point is in spinal cord, meaning if, e.g., the left spinothalamic tract in the spinal cord is fucked up, we lose pain and temperature on the right side of the body below the lesion. - Decussation point is called anterior white commissure. A lesion at this point is called syringomyelia, where there is bilateral loss of pain and temperature below the lesion.
Corticospinal tract	<ul style="list-style-type: none"> - Motor function from ipsilateral body.

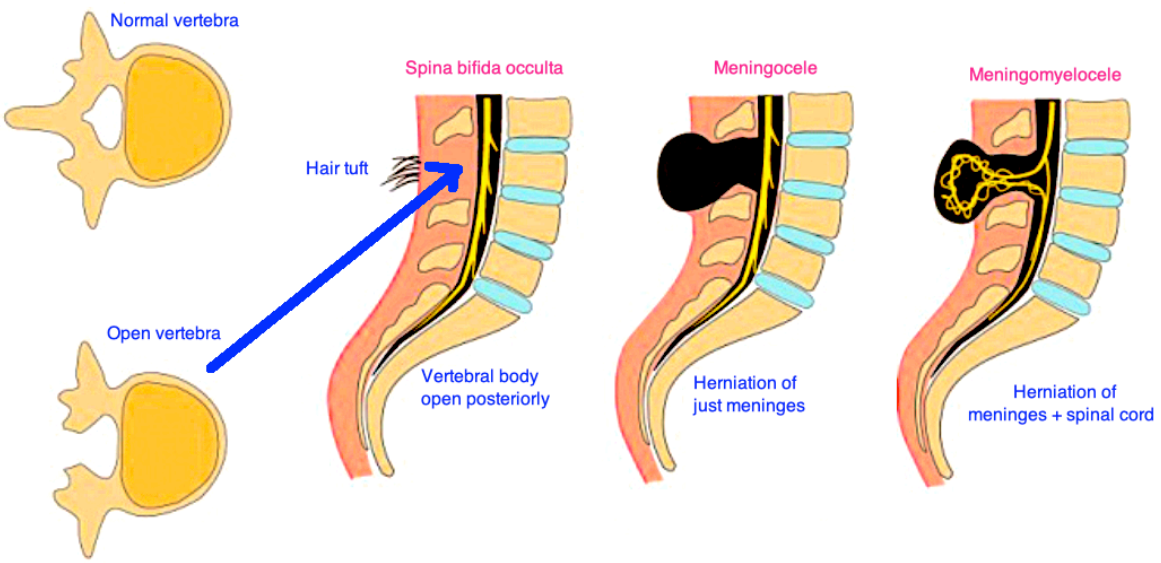
	- In other words, if left-sided corticospinal tract is fucked up, we lose motor function on the left side below the lesion.
Dorsal columns	<ul style="list-style-type: none"> - Carry vibration + proprioception from ipsilateral body. - Tabes dorsalis is dorsal column lesion caused by neurosyphilis. - If the dorsal columns are disrupted, patient will have (+) Romberg test, which is where he/she falls over when standing with eyes closed. I discuss this more below.

Upper- vs lower motor neuron findings	
UMN	<ul style="list-style-type: none"> - Lesion of the corticospinal tract (i.e., lesion from the cerebral cortex down until the anterior horn in the spinal cord). - Present as hyperreflexia, hypertonia, clonus, Babinski sign.
LMN	<ul style="list-style-type: none"> - Lesion involving the motor neuron from the anterior horn until the muscle itself. If the USMLE gives you an anterior horn lesion, this will be LMN, not UMN. - Present as hyporeflexia, hypotonia/flaccidity, fasciculations.

HY Spinal conditions	
Tabes dorsalis	<ul style="list-style-type: none"> - Loss of dorsal columns due to neurosyphilis.  <p>Myelin stain used, where normal myelination appears black. The dorsal columns are fucked up here, which is why they're white.</p> <ul style="list-style-type: none"> - Bilateral loss of vibration + proprioception. - Ataxia with (+) Romberg test → indicates dorsal columns are fucked up as the cause of the ataxia, since proprioception is lost. In contrast, if the cause of ataxia is cerebellar, for instance, Romberg test is (-).
Syringomyelia	<ul style="list-style-type: none"> - 9/10 Qs will give bilateral loss of pain and temperature due to lesion of anterior white commissure (decussation point for spinothalamic tract).

	 <p>Cyan dot marks the anterior white commissure.</p> <ul style="list-style-type: none"> - Maybe 1/3 of Qs will also involve corticospinal tract, where you'll see some impaired motor function in addition to the bilateral loss of pain/temperature. - 1/10 Qs will not mention pain/temperature loss but instead just give impaired motor function, where it sounds nothing like syringomyelia, but you're forced to eliminate to get there (on a 2CK Neuro CMS form).
Brown-Sequard syndrome	<p>- Hemisection of spinal cord.</p>  <p>Brown-Sequard syndrome</p> <ul style="list-style-type: none"> - Ipsilateral loss of vibration + proprioception (dorsal columns). - Ipsilateral loss of motor function (corticospinal tract). - Contralateral loss of pain + temperature (spinothalamic). - Not typically caused by stab wound where half the spinal cord is perfectly transected. It's to my observation on NBME forms (especially 2CK Neuro CMS) that they like viral infection or SLE causing transverse myelitis.
Transverse myelitis	<ul style="list-style-type: none"> - Inflammation of spinal cord resulting in variable deficits. - As mentioned above, USMLE likes viral infection and SLE (autoimmune). - Brown-Sequard syndrome is one way transverse myelitis presents.
Central cord syndrome	<ul style="list-style-type: none"> - The answer when weakness in the upper limbs is greater than weakness in the lower limbs. - Typically follows hyperextension injury of the neck during whiplash in a rear-end MVA.
Anterior cord syndrome	<ul style="list-style-type: none"> - The answer when there's preservation of vibration/proprioception but loss of motor + pain/temperature, classically in patient with arterial disease. - In other words, everything but the dorsal columns is fucked up. Essentially the opposite of tabes dorsalis.

Brachial plexus injuries	
<ul style="list-style-type: none"> - Both can be caused in neonates by breech / traumatic labor. - Can also be caused by injuries such as grabbing onto tree branch while falling. 	
Klumpke	<ul style="list-style-type: none"> - Lower brachial plexus injury (C8-T1). - Sometimes rather than Klumpke written as the diagnosis, the answer will just be "lower brachial plexus" when they ask for what's injured. 
Erb-Duchenne	<ul style="list-style-type: none"> - Upper brachial plexus injury (C5-C6). - Sometimes rather than Erb-Duchenne written as the diagnosis, the answer will just be "upper brachial plexus" when they ask for what's injured.  <ul style="list-style-type: none"> - Arm is adducted, pronated, and wrist flexed.

Spina bifida	
<p style="text-align: center;">Spina bifida types</p> 	
<ul style="list-style-type: none"> - HY point is that neural tube defects (spina bifida) occur between 3-4 weeks gestation. - The pregnant woman needs adequate folic acid (vitamin B9) prior to and during early pregnancy for prevention. - Antiepileptics (i.e., particularly valproic acid, but also phenytoin and carbamazepine) are also associated with neural tube defects. - Neural tube defects lead to increased AFP and acetylcholinesterase in CSF. 	

Neurogenic joint	
<ul style="list-style-type: none"> - Aka Charcot joint, where patient injures joint due to lack of joint sensation from peripheral neuropathy. - Usually seen in diabetes; can also be seen in neurosyphilis. - The answer on USMLE when they say diabetic patient has “disorganization of the tarsometatarsal joints” on foot x-ray. 	

Mononeuritis multiplex	
<ul style="list-style-type: none"> - Weird neuropathy that means neuropathy of “one large nerve in many locations” – e.g., wrist drop + foot drop in same patient. - Presents in patients with one of the vasculitides (i.e., Wegener, Churg-Strauss, microscopic polyangiitis). - In other words, you’ll get a vignette of Wegener, and then you’re like, “Wait, why does he/she have wrist drop though?” That’s just mononeuritis multiplex. 	
Granulomatosis with polyangiitis	<ul style="list-style-type: none"> - Formerly known as Wegener granulomatosis. - Answer on USMLE for adult with triad of 1) hematuria, 2) hemoptysis, and 3) “head-I” – i.e., any problem with the head, such as nasal septal perforation, mastoiditis, sinusitis, otitis. - Associated with cANCA and anti-proteinase 3 (anti-PR3) antibodies. - Causes “necrotizing glomerulonephritis” that can lead to rapidly progressive glomerulonephritis (RPGN).
Eosinophilic granulomatosis with polyangiitis	<ul style="list-style-type: none"> - Formerly known as Churg-Strauss. - Presents as combo of asthma + eosinophilia +/- head-I. - Head-I always seen in Wegener vignettes, but maybe only ~50% of CS Qs. - Renal involvement rare for CS. - Associated with pANCA and anti-myeloperoxidase (anti-MPO) antibodies.
Microscopic polyangiitis	<ul style="list-style-type: none"> - Will just present as hematuria in a patient who is pANCA / anti-MPO (+). - Similar to Wegener, can cause RPGN.

Hydrocephalus	
Communicating	<ul style="list-style-type: none"> - CSF can flow freely between the ventricles and subarachnoid space around the brain and spinal cord. - The answer for meningitis causing hydrocephalus, where the mechanism is “failure of CSF reabsorption by the arachnoid granulations.”
Non-communicating	<ul style="list-style-type: none"> - Aka obstructive hydrocephalus. - When there is a blockage preventing flow of CSF between the ventricles or subarachnoid space. - There is an NBME Q where they give a tumor of the spinal cord in the setting of hydrocephalus, and the answer is obstructive hydrocephalus. - Can be caused by aqueductal stenosis (narrowing of the cerebral aqueduct of Sylvius between the 3rd and 4th ventricles), which is the most common cause of congenital hydrocephalus. - Can be caused by colloid cyst, which is a benign fluid-filled growth at the anterior roof of the third ventricle, just posterior to the foramen of Monro.
NPH	<ul style="list-style-type: none"> - Normal pressure hydrocephalus. - “Wet, wobbly, wacky” +/- Parkinsonism. - In other words: urinary incontinence, ataxia, and cognitive dysfunction. - Due to impingement on the corona radiata (asked on an NBME), which is a white-matter bundle that connects the motor cortex superiorly to the internal capsule inferiorly. - Mechanism for urinary incontinence = “failure to inhibit the voiding reflex.”
Congenital	<ul style="list-style-type: none"> - Aqueductal stenosis is most common cause. - Most important cause on NBME, in my opinion however, is congenital toxoplasmosis, which presents as a triad of 1) hydrocephalus, 2) chorioretinitis, and 3) intracranial calcifications.

Ex-vacuo	<ul style="list-style-type: none"> - Appearance of enlarged lateral ventricles on imaging without true hydrocephalus. - Can be caused by loss of surrounding brain matter. - Alzheimer and schizophrenia are important causes on USMLE, where enlargement of the lateral ventricles is a finding that can sometimes show up in question stems.
----------	---

HY dementia types	
Alzheimer	<ul style="list-style-type: none"> - Gradual-onset idiopathic cognitive decline. - Patient must have normal neurologic exam (i.e., no motor or sensory abnormalities). - MMSE score will be low (i.e., low-20s out of 30) on USMLE. If the diagnosis is instead benign senility, USMLE will give MMSE usually 28+. - Beta-amyloid plaques and neurofibrillary tangles (hyperphosphorylated tau protein) seen on brain biopsy. - Early-onset Alzheimer in Down syndrome (amyloid precursor protein gene is located on chromosome 21). - Presenilin gene mutations can cause Alzheimer (on NBME exam). Presenilin is a protein involved in the cleavage of amyloid. - Tx = cholinesterase inhibitors (donepezil, galantamine, rivastigmine); memantine (NMDA glutamate receptor antagonist) can also be used. - Sundowning is worsening of dementia at night that can resemble delirium. - 1st-line Tx for sundowning on NBME is "decrease ambient noise and distractions." - "Bright illumination of the room at all times" is wrong answer.
Frontotemporal dementia	<ul style="list-style-type: none"> - Aka Pick disease. - Presents usually as triad of 1) personality change, 2) apathy, and 3) disinhibition. - Accumulation of hyperphosphorylated tau protein (similar to Alzheimer), except rather than accumulating as neurofibrillary tangles, it accumulates as round, silver-staining inclusions known as Pick bodies.
Lewy body dementia	<ul style="list-style-type: none"> - Dementia + visual hallucinations + Parkinsonism. - Lewy bodies are collections of alpha-synuclein. This protein is deposited throughout the brain in Lewy-body dementia. In Parkinson disease, in contrast, it is deposited primarily in the substantia nigra pars compacta of the midbrain.
Vascular dementia	<ul style="list-style-type: none"> - Aka multi-infarct dementia. - The answer for dementia + motor/sensory abnormalities. - Seen in patients who have repeated mini-strokes (cerebral infarcts) due to hypertension. - Resources tend to focus on this notion of "step-wise decline" (i.e., concrete timepoints at which deficits started), but it's to my observation on NBME exams that this is rarely a salient aspect of Qs. What USMLE likes is giving motor and/or sensory deficits – i.e., you'll get a big paragraph with dementia, and you'll notice somewhere in the stem that the patient has, e.g., 3/5 strength in the right upper extremity. This indicates Hx of stroke.
AIDS	<ul style="list-style-type: none"> - Just be aware AIDS can cause dementia, known as AIDS complex dementia. - Can present as "wet, wobbly, wacky," similar to normal pressure hydrocephalus.
Pseudodementia	<ul style="list-style-type: none"> - Not actual dementia. This is depression that presents as cognitive decline. - Patients with depression who have apathy will perform poorly on the MMSE. - The Q might say the patient is unable to draw a clockface, but when prompted, is able to finish it quickly. They might also say patient remembers 0 out of 3 objects after 5 minutes. - Look for obvious signs of depression, such as short, quiet answers, and low mood.
Subacute combined degeneration	<ul style="list-style-type: none"> - The fancy name for neurologic degeneration seen in B12 deficiency. - Can present sometimes as a reversible cause of dementia. In elderly patients on tea and toast diets, or those in high-risk groups (i.e., vegans, pernicious anemia), B12 must be considered as cause of cognitive decline.

	<ul style="list-style-type: none"> - The patient can have peripheral neuropathy as a result of deficits to the 1) corticospinal tracts, 2) dorsal columns, and 3) spinocerebellar tracts. - The easy way to remember those three is to start by saying, "The spinothalamic tract is not involved." Then you say, "Well what are other ones I can think of?"
Neurosyphilis	<ul style="list-style-type: none"> - Just be aware that neurosyphilis is a reversible cause of dementia and should be considered. There's an NBME Q floating around for 2CK where they give (+) VDRL in 82-year-old woman with cognitive decline, and the treatment is penicillin.

Parkinson disease / Parkinson-plus disorders	
- A Parkinson-plus disorder is a disease that presents similarly to Parkinson disease, but it's not.	
Parkinson disease	<ul style="list-style-type: none"> - Loss of dopamine-secreting neurons in the pars compacta of the midbrain, with deposition of alpha-synuclein on biopsy. - Presents with classic features of bradykinesia/akinesia, resting tremor, shuffling, short-stepped gait, micrographia, and cogwheel rigidity. - Alpha-synuclein gene mutation most common; many genes implicated. - Carbidopa-levodopa is combo frequently used for Tx. Levodopa crosses the BBB to be converted to dopamine centrally. However, levodopa is subject to fast metabolism when administered alone. The addition of carbidopa functions as a competitive inhibitor of breakdown enzymes, resulting in increased levodopa availability for passage across the BBB. Do not confuse this mechanism with direct COMT inhibitors (tolcapone, entacapone), which prevent breakdown of L-dopa. - Carbidopa-levodopa can cause psychosis if administered in too-high a dose. This is assessed on 2CK Psych forms, where if patient gets psychotic episodes following recent addition of C-L to regimen, or following an increase in dose, the answer is simply "decrease dose of carbidopa-levodopa." "Discontinue carbidopa-levodopa is the wrong answer." - Be aware of D2 agonist names – i.e., ropinirole, pramipexole, cabergoline, pergolide, and bromocriptine, which can all in theory be used as treatments. - Amantadine increases presynaptic release of dopamine. - Selegiline inhibits monoamine oxidase B, which is an enzyme that preferentially breaks down dopamine. USMLE wants you to know this can cause serotonin syndrome, either alone, or in combo with drugs like St John Wort or SSRIs.
RLS	<ul style="list-style-type: none"> - Restless leg syndrome. - Idiopathic, irresistible urge to move legs while in bed/sleeping. - Most common cause is iron deficiency anemia. First step is checking the patient's serum iron and ferritin. - If iron studies are normal, gabapentin and D2 agonists (ropinirole, pramipexole) can be used. - USMLE wants you to know that patients with RLS have increased risk of developing Parkinson disease, which makes sense since D2 agonists help, indicating a potential problem with dopamine signaling or production in some patients.
NPH	<ul style="list-style-type: none"> - As discussed earlier, normal pressure hydrocephalus presents as "wet, wobbly, wacky" +/- Parkinsonism. - The parkinsonism is the most overlooked detail by students, who will usually only know the wet, wobbly, wacky part. - What the USMLE will do is give you an older male who has WWW triad + they give you 2-3 more sentences describing what sounds like Parkinson disease, where you're like "What the hell? Is this Parkinson disease?" No. It's just NPH, which is a Parkinson-plus disorder, where it can look like Parkinson disease but it ain't. - Once again, due to impingement on the corona radiata, and the mechanism they want for urinary incontinence = "failure to inhibit the voiding reflex."
Wilson disease	<ul style="list-style-type: none"> - Parkinsonism in a young patient is Wilson disease till proven otherwise. - Excessive copper accumulation in tissues, including the basal ganglia and liver, due to inability to excrete it into bile.

	- I discuss this stuff in more detail in the HY Gastro PDF.
Lewy body dementia	- As discussed before, this is a Parkinson-plus disorder. - The patient will have dementia + visual hallucinations + Parkinsonism.
Progressive supranuclear palsy	- Obscure condition that gets asked on 2CK. - You just need to know that 100% of questions will say "axial dystonia + Parkinsonism," where they'll just ask for diagnosis straight-up. - Axial dystonia is a type of muscle condition resulting in abnormal posture and movement of the spine and torso.
MPTP	- Aka synthetic heroin. - Just know it is a cause of Parkinsonism. - Shows up on a 2CK Psych form. Students are like wtf?

MLF syndrome

- Medial longitudinal fasciculus syndrome (MLF syndrome; aka internuclear ophthalmoplegia; INO).
- Pathognomonic for multiple sclerosis. MS patients can also get optic neuritis (as mentioned above), but this is not pathognomonic for MS (i.e., it can be seen in other circumstances, such as with ethambutol or sildenafil use).
- Mechanism for pathology: when you look to one side (let's say the right), CN VI on the right and CN III on the left are activated. This union of activation is accomplished when the left MLF in the midbrain is activated. In the case of MLF syndrome, the right eye can abduct without a problem, but the left eye will fail to adduct, and the right eye will exhibit nystagmus back toward the midline.
- What you need to remember is: in INO, the side that cannot adduct is the side that's fucked up. So if you look to the right and the left eye doesn't adduct, then the left MLF is where the lesion is.

Internuclear ophthalmoplegia (INO), aka Medial longitudinal fasciculus (MLF) syndrome



Normal patient



Patient with L-sided INO



Normal eye will demonstrate
nystagmus toward midline →

Cannot adduct when
contralateral CN VI
activated



Patients with INO can
converge normally

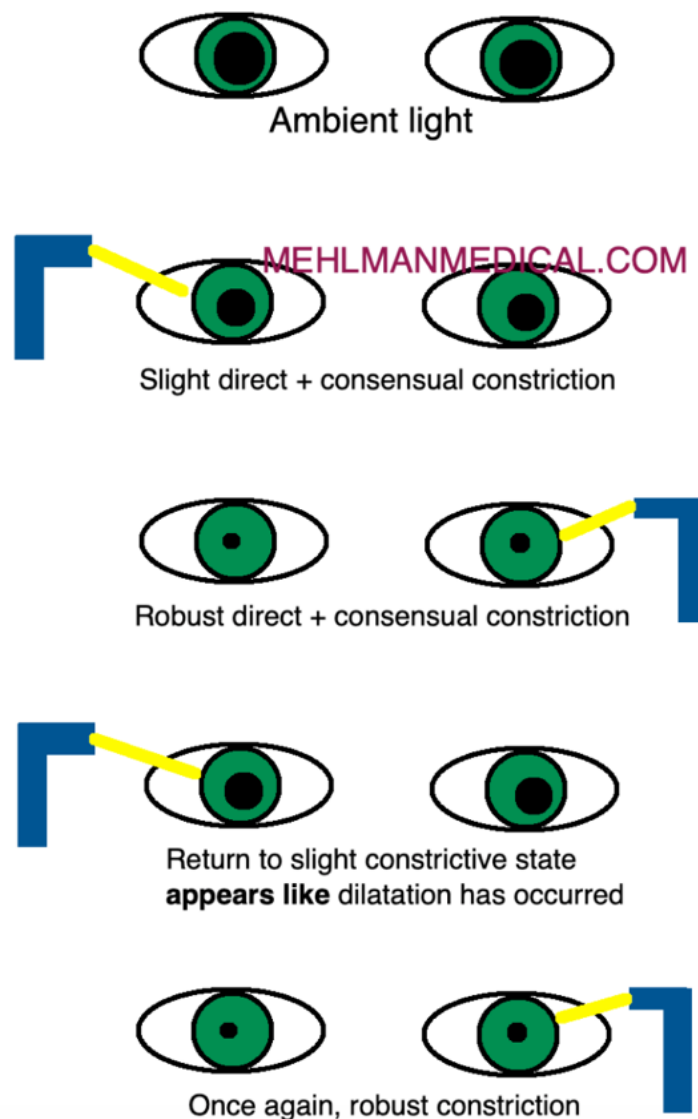
Patients with CN III
lesion cannot converge

Optic neuritis

- Inflammation of CN II (optic nerve) that presents variably as change in visual acuity, color vision, central scotoma, etc., and **is basically always seen in multiple sclerosis on USMLE**. I discuss MS more later.

- Causes Marcus Gunn pupil (aka relative afferent pupillary defect). In this case, the intensity of light is under-sensed by the affected eye (afferent signal), so the resultant efferent CN III (oculomotor) parasympathetic output (back to the eyes for pupillary constriction) is attenuated; this means when you shine a light in the affected eye, both pupils constrict less in comparison to when the light is shone in the unaffected eye; this **gives the mere impression** that the pupils dilate when light is shone in the affected eye. Still confusing? Take a look at the following illustration (assuming a lesion of the patient's right eye [left side of illustration]):

Relative afferent pupillary defect (Marcus Gunn pupil)



Autoimmune neuropathies	
Multiple sclerosis	<ul style="list-style-type: none"> - T-cell-mediated attack against oligodendrocytes and myelin-basic protein. - Idiopathic autoimmune disorder classically in white women 20s-30s who live far from the equator. - Relapsing-remitting type is most common, where the patient will have repeated episodes of neurologic disturbances over many years at varying intervals. - Highest yield findings are optic neuritis and INO, as discussed above. - Urge incontinence is exceedingly HY. Some students ask about overflow incontinence due to MS; I've never seen this on NBME. Urge incontinence is what shows up all over the NBME forms for MS. - MRI is gold standard for diagnosis, showing scattered white matter lesions within the CNS (i.e., both brain and spinal cord). - CSF analysis shows IgG oligoclonal bands. - Clonus and (+) Babinski sign (UMN findings) also HY. - Tx is steroids for acute flares (IV methylprednisolone). - β-interferon is what USMLE wants between flares to decrease recurrences. - Baclofen (GABA-B receptor agonist) is used for spasticity.
Neuromyelitis optica	<ul style="list-style-type: none"> - Aka Devic disease. - Sounds exactly like MS but they will say CSF oligoclonal bands are negative, and then the answer is just "antibodies against aquaporin-4." - You say Wtf? Not my opinion. It's asked on a 2CK form.
ALS	<ul style="list-style-type: none"> - Amyotrophic lateral sclerosis. - In ALS, the lateral corticospinal tracts (UMN) and anterior horns (LMN) degenerate. - There are two things you will see in all ALS Qs, making the Dx very easy: <ol style="list-style-type: none"> 1) The vignette will always have combination of UMN and LMN findings. Fasciculations, decreased reflexes, decreased tone, and muscle atrophy are classic for LMN. Babinski reflex, clonus, increased (brisk) reflexes, increased tone are classic for UMN. Serum CK can be elevated due to increased tone. 2) Must have no sensory findings. If any sensory abnormalities (i.e., paresthesias, numbness, etc.) are present in the vignette, ALS is the wrong answer. - USMLE will often give vignette of ALS and then the answer is simply "motor neurons." - Knowing this second point in particular will help on difficult 2CK Qs, where you'll get a big paragraph + they say somewhere in the stem something about a sensory abnormality, and you can say, "Cool, not ALS." - For 2CK, next best step in Dx = "electromyography and nerve conduction studies."
GBS	<ul style="list-style-type: none"> - Guillain-Barre syndrome (aka acute inflammatory demyelinating polyneuropathy). - T-cell- and antibody-mediated destruction of Schwann cells and myelin of peripheral nerves. - In other words, MS = CNS/oligodendrocytes; GBS = PNS/Schwann cells. - Can be described as "segmental and inflammatory demyelination." - Presents as ascending paralysis and loss of deep tendon reflexes. - Can affect both upper and lower limbs. - Symptoms can start as tingling in the hands and/or feet. - USMLE can say "weakness of proximal and distal muscles in lower limbs and weakness of distal muscles in upper limbs" → the implication is that the weakness has already ascended in the legs but not yet in the arms. - Textbook cause is <i>Campylobacter jejuni</i>, but in almost all Qs they will not give a patient who has bloody diarrhea after a BBQ. In other words, you can't use this as a crutch. They will just give you the symptoms alone and you have to know it's GBS.
CIDP	<ul style="list-style-type: none"> - Chronic inflammatory demyelinating polyneuropathy. - Vignette will sound exactly like GBS, but symptoms will be present for months and progress slowly. - GBS, in contrast, develops quickly over days and peaks within weeks.

	<ul style="list-style-type: none"> - In other words, if you get a vignette where it sounds like GBS, but they say the symptoms have been present for 4 months, that's CIDP, not GBS. There's one Q on a 2CK form on it.
CMTD	<ul style="list-style-type: none"> - Charcot-Marie-Tooth disease. - Obscure peripheral nerve autoimmune disease that is the answer on USMLE if they give you high-arched feet (pes cavus), hammer toes, and foot drop.
Bell's palsy	<ul style="list-style-type: none"> - LMN lesion of CN VII (facial nerve). - Paralysis of ipsilateral facial muscles. - Usually idiopathic/autoimmune following viral infection, shingles (i.e., Ramsay-Hunt syndrome II), or Lyme disease. - If the Q gives you Bell's palsy and asks for next best step, the answer is do serology for Lyme disease. If this isn't listed (or the patient doesn't live in endemic area, such as Africa), choose "no further diagnostic studies indicated." Nerve conduction studies are wrong (this is on NBME). Bell's palsy is a clinical diagnosis. - IV steroids, followed by a 10-21-day taper of oral steroids is indicated to minimize the immune response. - Ipsilateral hyperacusis (due to paralysis of stapedius muscle) and/or loss of taste to the anterior 2/3 of the tongue are basically nonexistent in questions. - There is a Q on NBME where they say patient has loss of taste following trauma + neurologic exam shows no abnormalities → answer = olfactory nerve (CN I) palsy, not CN VII, due to cribriform plate fracture (loss of smell means loss of most taste). If the Q wanted CN VII lesion, they would give a concurrent Bell's palsy presumably, since loss of taste wouldn't happen in isolation with CN VII palsy. - In contrast to CN VII lesion that is 19 times out of 20 LMN causing Bell's palsy, you should be aware that 1/20 are UMN, which results in loss of motor function of the contralateral middle and lower face, with the forehead spared.
PANDAS	<ul style="list-style-type: none"> - Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococci. - In rare cases, Group A Strep pharyngitis can cause a tic disorder, OCD, or ADHD in the weeks following infection. - USMLE will give you kid who had sore throat two weeks ago + now has a new-onset tic, ADHD, or OCD, and they will ask what will most likely diagnose etiology for the disorder → answer = "anti-streptolysin O titers."
Sydenham chorea	<ul style="list-style-type: none"> - Autoimmune movement disorder seen as part of rheumatic fever. - Chorea = fast, purposeless, jerky movements. - Vignette will give child who has rheumatic fever and then ask about the cause of the movement disorder, and the answer is just "autoimmune." - I discuss rheumatic heart disease in detail in the HY Cardio PDF.
Myoneural junction disorders	
Myasthenia gravis	<ul style="list-style-type: none"> - Autoantibodies against post-synaptic nicotinic acetylcholine receptors. - Classic vignette is female office worker in her 40s who has triad of 1) diplopia, 2) dysphagia, and 3) ptosis that worsens throughout the day. - Gets worse with recurrent stimulation of muscle (vignette might say the patient cannot perform upward gaze for 60 seconds). - Tensilon test is administration of edrophonium (short-acting acetylcholinesterase inhibitor) → patient experiences significant improvement in symptoms. - Tx = pyridostigmine (longer-acting acetylcholinesterase inhibitor). - MG can be a paraneoplastic syndrome of thymoma. - 10-15% of patients with MG have thymoma. - If MG is diagnosed, a chest x-ray should be performed to look for thymoma. If the x-ray is abnormal, a CT scan is ordered. - Removal of the thymoma in these patients can significantly improve/cure the MG.
Lambert-Eaton	<ul style="list-style-type: none"> - Autoantibodies against pre-synaptic voltage-gated calcium channels. - Presents as proximal muscle weakness that improves with activity (vignette might say the patient tries to get up from a chair a few times before finally being able to). - Tensilon test does not significantly improve Sx in comparison to MG. - Highest-yield point is that it is a paraneoplastic syndrome of small cell lung cancer.

Vertigo	
BPPV	<ul style="list-style-type: none"> - Benign paroxysmal positional vertigo. - Vertigo is the feeling of the room spinning. - Brief episodes of dizziness, usually 30-60 seconds, sometimes with vomiting. - Caused by a semicircular canal otolith (ear stone; aka otoconia). - Otoconia made of calcium carbonate are normally found within the utricle and saccule of the inner ear and play a role in detecting acceleration and motion. If one becomes dislodged and enters the semicircular canals, BPPV results. - Diagnosis is made via Dix-Hallpike maneuver. In this test, nystagmus is induced when the patient is rapidly moved from a seated position to lying down with the head tilted backward and turned to one side. If nystagmus occurs, Dx = BPPV. - Tx is Epley maneuver, which is a series of head movements aimed at moving the semicircular canal otolith back to the utricle, thereby curing the BPPV.
Vestibular neuritis	<ul style="list-style-type: none"> - Viral infection + vertigo. - Inflammation of the vestibular nerve (branch of CN VIII, vestibulocochlear nerve).
Labyrinthitis	<ul style="list-style-type: none"> - Viral infection + vertigo +/- tinnitus. - Inflammation of both the vestibular nerve and cochlear nerve. - This distinction of "VN is just vertigo whereas labyrinthitis is also tinnitus" is perpetuated on the internet, but I can tell you there is an NBME Q (that is repeated across forms) where they don't mention anything about tinnitus and the answer is labyrinthitis (where vestibular neuritis isn't listed). This is why I write "+/-" for tinnitus above. - The tympanic light reflex can be abnormal, which can reflect increased middle ear pressure (sometimes seen with viral infection). I've seen the NBME write in the stem "abnormal light reflex," which is a confusing point, since this could be misconstrued as referring to the eyes, not the ear. The vignette in which they mention this they also have multiple sclerosis as a wrong answer + mention the patient has a sibling with MS. So the Q is dumb/gotcha-style overall. The key sentence in this NBME Q is that the patient had nausea and reduced ability to eat foods past few days, which implies recent viral infection.
Meniere	<ul style="list-style-type: none"> - Waxing and waning, asymmetric tinnitus and vertigo that has a slowly progressive course over many years. - Has a familial component but no strict inheritance (i.e., the vignette can sometimes mention a relative with similar findings). - Due to defective endolymphatic drainage. - Can cause low-frequency hearing loss (i.e., patient says it is difficult to hear conversations at the dinner table with many people). This is in contrast to presbycusis, which is high-frequency hearing loss in elderly.
Drug-induced	<ul style="list-style-type: none"> - Aminoglycosides (i.e., gentamicin, amikacin), chemo agents like cisplatin, and loop diuretics (furosemide, ethacrynic acid) are known for ototoxicity. - Keep point is that this ototoxicity need not be hearing loss and can be vertigo – i.e., the patient is receiving IV Abx for endocarditis treatment and feels like the room is spinning (ototoxicity due to gentamicin).

HY headache types	
Trigeminal neuralgia	<ul style="list-style-type: none"> - 11/10 lancinating, knife-like pain that occurs as episodes lasting usually <1 minute. - Classically brought on by minor stimuli, such as brushing one's hair/teeth, or a gust of wind. - Thought to be caused by trigeminal nerve irritation or impingement (i.e., at the exit points from the skull).

	<ul style="list-style-type: none"> - There is an NBME Q where they ask what part of the brain is fucked up (i.e., they don't list any nerves), and the answer is pons, since CN V originates from the pons. - Prophylaxis is carbamazepine. - There is no Tx for acute episodes since pain lasts such short duration. - Often confused with cluster headache if occurring in the V1 (ophthalmic branch of trigeminal nerve) distribution.
Cluster headache	<ul style="list-style-type: none"> - Male 20s-40s who wakes up from sleep with 11/10 lancinating, knife-like headache; often associated with ipsilateral lacrimation, rhinorrhea, and sometimes pupillary changes (I've seen NBME say ipsilateral miotic pupil). - Episodes last minutes to half hour (longer than trigeminal neuralgia), where the Q will say the guy wakes up from sleep + paces around his room until pain eventually goes away. - Prophylaxis is verapamil. - Tx for acute episodes is oxygen (bizarre, unless patient has O2 tank lying around).
Migraine	<ul style="list-style-type: none"> - Unilateral throbbing/pounding headache that lasts hours. - Can be associated with prodromal visual aura or sounds. - Prophylaxis is propranolol. - Tx is NSAIDs first, followed by triptans (e.g., sumatriptan). - Triptans are serotonin (5HT) receptor agonists. - Triptans are not prophylactic meds; they are only used as abortive therapy. - USMLE will give 30s female with hypertension who has migraine Hx, and the treatment is "beta blockade" for her HTN management. - Estrogen-containing contraceptives are contraindicated in patients who have migraine with aura.
Tension headache	<ul style="list-style-type: none"> - Bilateral, dull, band-like headache. - Treated with sleep and acetaminophen.
Temporal arteritis	<ul style="list-style-type: none"> - Aka giant cell arteritis. - 9/10 Qs will be painful unilateral headache in patient over 50. I've seen one Q on NBME where it's bilateral. - Flares can be associated with low-grade fever and high ESR. - Patients can get proximal muscle pain and stiffness. This is polymyalgia rheumatica (PMR). The two do not always go together, but the association is HY. (Do not confuse PMR with polymyositis. The latter will present with ↑ CK and/or proximal muscle weakness <i>on physical exam</i>. PMR won't have either of these findings. I talk about this stuff in detail my MSK notes.) - Patients can get pain with chewing. This is jaw claudication (pain with chewing). - Highest yield point is we give steroids before biopsy in order to prevent blindness. - An NBME has "ischemic optic neuropathy" as the answer for what complication we're trying to prevent by giving steroids in temporal arteritis. - IV methylprednisolone is typically the steroid given, since it's faster than oral prednisone. - It's to my observation many 2CK NBME Qs will give the answer as something like, "Steroids now and then biopsy within 3 days," or "IV methylprednisolone and biopsy within a week." Students ask about the time frames, but for whatever reason USMLE will give scattered/varied answers like that. - Another 2CK Neuro CMS Q gives easy vignette of temporal arteritis and then asks next best step in diagnosis → answer = biopsy. Steroids aren't part of the answer. Makes sense, since they're asking for a diagnostic step.

WKS and ataxia	
- Ataxia is a neurological disorder characterized by a lack of coordination of voluntary muscle movements, leading to unsteady gait and difficulty with balance.	
WKS	<ul style="list-style-type: none"> - Wernicke-Korsakoff syndrome. - Damage to primarily the mamillary bodies due to thiamine (B1) deficiency.

	<ul style="list-style-type: none"> - Wernicke encephalopathy = A COW = Ataxia, Confusion, Ophthalmoplegia, Wernicke. - Korsakoff psychosis = retrograde amnesia; causes confabulations, which means making up stories about the past because of loss of memory regarding prior events. - Therefore, WKS = A COW + confabulations. - Application to USMLE is that alcoholics presenting to hospital with confusion, ataxia, or eye findings require thiamine. - One NBME Q asks what giving thiamine will help reduce risk of in alcoholic → answer = anterograde amnesia (apparently by reducing risk of confusion due to Wernicke), where retrograde amnesia isn't listed as answer.
General Ataxia	<ul style="list-style-type: none"> - USMLE wants you to be able to differentiate ataxia caused by cerebellar vs dorsal column lesions. - Dorsal column lesions cause a (+) Romberg test, meaning the patient falls over when standing with the eyes closed due to loss of proprioception. - Cerebellar lesions won't cause a (-) Romberg test almost always due to maintenance of proprioceptive capacity.
Ataxia-telangiectasia	<ul style="list-style-type: none"> - X-linked Immunodeficiency condition that causes – you'd never guess it – ataxia and telangiectasias. What USMLE will do is make the diagnosis obvious, and then the answer will just be “failure of double-stranded DNA break repair.”

Cerebellar lesion signs	
Asterixis	<ul style="list-style-type: none"> - Aka “hepatic flap.” - Motor disturbance characterized by brief, sudden lapses of muscle tone, presenting as the patient demonstrating a “flapping” motion of the hands when he or she extends the arms and hands anteriorly.
Dysidiadokokinesia	<ul style="list-style-type: none"> - Impaired ability to perform rapid alternating movements; presents as difficulty rapidly tapping a finger or quickly pronating and supinating the hand.
Intention tremor	<ul style="list-style-type: none"> - Kinetic tremor that worsens as the patient's hand approaches a target.
Truncal ataxia	<ul style="list-style-type: none"> - Tends to occur with more midline cerebellar lesions (i.e., of the vermis). - Can be seen, e.g., in pediatrics with medulloblastoma, where a kid has morning vomiting (often indicates brain tumor) and truncal ataxia.
Limb ataxia	<ul style="list-style-type: none"> - Tends to occur with more lateral cerebellar lesions. - An important rule is that cerebellar lesions cause ipsilateral deficits, unlike many brain lesions that cause contralateral limb findings.

Neuro conditions caused by vitamin deficiencies	
Vit B12	<ul style="list-style-type: none"> - As discussed earlier, causes subacute combined degeneration, with reversible dementia and/or systemic neurologic findings. - Hx of gastrectomy, pernicious anemia, veganism, or strict vegetarianism is buzzy. - If patient has B12 deficiency + an unrelated autoimmune disorder, e.g., vitiligo, Hashimoto, etc., the cause is probably pernicious anemia, since “autoimmune diseases go together,” where having one autoimmune disease ↑ risk of others. - Patients need not have neurologic dysfunction in B12 deficiency. This is a common misconception. - Causes ↑ MCV (megaloblastic anemia) and hypersegmented neutrophils. - If Q gives you older patient on tea and toast diet + high MCV + no other information, folate (B9) deficiency is more common than B12 deficiency (on NBME).
Vit B1	<ul style="list-style-type: none"> - Can cause WKS, dry beri beri (neuropathy), and wet beri beri (dilated cardiomyopathy). - Two new 2CK NBME Qs assess thiamine deficiency causing neuropathy (dry beri beri) <i>post-gastrectomy</i>, which is bizarre, since we classically think of this as causing B12 deficiency. - A helpful detail that B1 deficiency is the answer post-gastrectomy instead of B12 is if they give <i>confusion</i>, which is characteristic of Wernicke encephalopathy, not subacute combined degeneration.

	- One of the Qs also mentions a (+) Romberg test for B1 deficiency as well. Everyone gets these Qs wrong because the notion of B1 deficiency as correct post-gastrectomy, as opposed to B12, is recondite and obscure.
Vit E	- Can cause peripheral neuropathy. - Weirdly an extremely HY vitamin deficiency on USMLE, despite it not seeming that common. Shows up in cystic fibrosis questions . - Patients with CF have exocrine pancreatic insufficiency leading to fat-soluble vitamin malabsorption. So CF patient + neuropathy = vitamin E deficiency. - Can in theory be seen with any cause of exocrine pancreatic insufficiency (i.e., chronic pancreatitis due to alcoholism, pancreatectomy, severe diabetes), but it's HY for CF Qs as I said. - Likewise, bowing of tibias / low Ca^{2+} in CF patients would be vitamin D deficiency.
Vit B6	- Neuropathy and/or seizures in patients taking isoniazid for tuberculosis.

Tremor types for IM	
Essential	- Autosomal dominant intention tremor. - Can occur at any age, but usually middle age and older. - Patients self-medicate with alcohol, which ↓ tremor. - Propranolol (beta-blockade) is treatment.
Resting	- Parkinson disease (or Parkinson-plus disorder) in older patients. - Wilson disease till proven otherwise in younger patients.
Intention	- Cerebellar lesions or essential tremor.
Drug-induced	- Lithium and valproic acid can both cause tremor. - Lithium is classic for tremor, but an NBME Q gives valproic acid as correct answer (and lithium wrong answer) for patient who has tremor + abnormal liver function tests, since valproic acid is known for hepatotoxicity but lithium is not. - Albuterol (β_2 -agonist for asthma) shows up in an NBME Q as causing tremor. - Alcohol withdrawal (delirium tremens). Treat with benzo.

Meningitis	
- Presents as high fever + stiff neck and photophobia.	
Bacterial	- Usually Group B Strep in neonates (gram-positive cocci). - <i>S. pneumo</i> and <i>N. meningitides</i> most common otherwise. - CSF shows ↑ Protein, ↓ glucose, ↑ neutrophils (polymorphonuclear cells).
Fungal	- <i>Cryptococcus neoformans</i> in immunocompromised patients (i.e., HIV). - CSF shows ↑ Protein, ↓ glucose, ↑ lymphocytes.
Viral	- Aka aseptic meningitis. - Commonly echovirus (if vaccinated); can also be mumps (if unvaccinated). - CSF shows normal protein (or a tad elevated), normal glucose, ↑ lymphocytes.
Encephalitis	
- Presents as high fever + confusion .	
HSV 1/2	- Herpes encephalitis can occur following vertical transmission. - RBCs in the CSF due to temporal lobe hemorrhage. - Non-contrast CT of the head is often negative, so don't be confused by this. However they can say EEG shows abnormal spikes over the temporal region. - Other CSF findings same as viral meningitis. - I've only ever seen one NBME Q on 2CK Neuro CMS form where RBCs were absent in CSF in herpes encephalitis, but you could still get the answer because other CSF findings were viral + no other virus listed.
Additional HY points	
- Do lumbar puncture before antibiotics, as the latter first can interfere with culture results. - Four indications for doing CT before LP in suspected meningitis / encephalitis: 1) Focal neurologic signs.	

2) Seizure.

3) Papilledema, or the optic fundi cannot be visualized.

4) Confusion that interferes with neurologic exam / reduced Glasgow score.

- The reason for CT before LP in the above scenarios is because of the risk of intracranial mass lesion, where if LP is performed, which acutely ↓ intracranial pressure, herniation and death might occur.

- 2CK NBME Q gives point #3 above, where answer is CT, not LP, and many students get it wrong.

- Empiric Tx for meningitis is ceftriaxone + vancomycin. Steroids can be added if confirmed *S. pneumo*.

- For Group B Strep only, choose ampicillin + gentamicin, or ampicillin + cefotaxime; the combo of vancomycin + ceftriaxone is wrong on the NBME for GBS.

- 2CK NBME Q has amp + gent as correct over vanc + ceftriaxone for GBS.

- We normally avoid ceftriaxone in the first month of life and prefer cefotaxime as the 3rd-gen cephalosporin. The exact age of the transition is not so important. What you need to know is, if you get a Peds Q and both cefotaxime and ceftriaxone are listed, cefotaxime is what we generally prefer.

- Ceftriaxone, compared to cefotaxime, displaces bilirubin from albumin, thereby ↑ risk of neonatal hyperbilirubinemia. It can also cause calcium deposits in the lungs and kidney.

- HY that you know meningitis can cause sensorineural hearing loss. If they tell you, e.g., 6-year-old boy isn't paying attention in class + isn't doing well in school + has Hx of meningitis; next best step = air-conduction audiometry. Do not confuse with tympanometry, which evaluates mobility of the tympanic membrane.

Other CNS infections

Toxoplasmosis	<ul style="list-style-type: none"> - <i>Toxoplasma gondii</i>; protozoan (unicellular eukaryote). - Causes ring-enhancing lesion(s) on CT head. - Doesn't need to be in patient who has exposure to cats. - Can be acquired from pork. - Prophylaxis is trimethoprim-sulfamethoxazole (TMP-SMX) in HIV patients with CD4 count <100/μL. - Since patients with HIV are already commenced on TMP-SMX for <i>Pneumocystis jirovecii</i> pneumonia (PJP) prophylaxis once CD4 count is <200, the latter functions as two birds with one stone for eventual Toxo prophylaxis. - It is important for USMLE that you know the prophylaxis for PJP and toxo is the same, since if they give you ring-enhancing lesion on CT in HIV patient with CD4 count <100 who's on TMP-SMX, you know it's not Toxo. In this case, the diagnosis is primary CNS lymphoma. - The treatment for toxo is sulfadiazine + pyrimethamine. This distinction is asked on a 2CK NBME, where TMP-SMX is also listed and wrong.
AIDS	<ul style="list-style-type: none"> - Can cause AIDS complex dementia, as discussed earlier. This presents as "wet, wobbly, wacky" (similar to NPH) in an AIDS patient. - Can cause primary CNS lymphoma, especially when CD4 count is <100/μL.
Neurocysticercosis	<ul style="list-style-type: none"> - <i>Taenia solium</i>; cestode; pork tapeworm. - Causes lesions within the brain in patient who went abroad, e.g., to Mexico. - Treated with albendazole or praziquantel.
Mastoiditis	<ul style="list-style-type: none"> - Complication of untreated or severe otitis media. - Q will tell you a child has tenderness behind the ear + the pinna is displaced upward and outward. - Next best step is CT or MRI of the temporal bone to visualize a potential fluid collection, since if this is not drained it can lead to brain abscess. - 2CK form has CT of temporal bone as answer for mastoiditis in a kid; sounds wrong to do head CT in a kid, but it's what they want on the form. - X-ray is wrong answer, as it doesn't adequately visualize a potential fluid collection.
Brain abscess	<ul style="list-style-type: none"> - Abscess in the brain. Not rocket science. - Can be caused by septic embolus due to endocarditis. - Q will give you murmur + fever + neurologic findings → vegetation from heart valve has launched off to the brain, causing stroke-like presentation. - Tx = drainage of abscess + IV antibiotics.

Epidural abscess	<ul style="list-style-type: none"> - Usually presents as “point tenderness over a vertebra,” which on USMLE means epidural abscess, compression fracture (osteoporosis), or metastases. - Patient may or may not have neurologic findings. Fever is not mandatory. - Three demographics I’ve seen on NBME exams for epidural abscess: <ol style="list-style-type: none"> 1) IV drug user who now has point tenderness over vertebra; 2) Patient who’s had some sort of cellulitis of the legs / lower body that has spread to the spine, where you’ve eliminated the other answers to get there; 3) Patient with active endocarditis (i.e., murmur + fever) who has neurologic findings in the legs (septic embolus also possible, but this tends to produce stroke-like findings rather than spinal pain + lower leg findings). - Tx = drainage of abscess + IV antibiotics.
Pott disease	<ul style="list-style-type: none"> - Infection / granulomatous destruction of the vertebral column by tuberculosis. - Just know that this is possible, the same was psoas abscess is also possible.
Rabies	<ul style="list-style-type: none"> - RNA virus that ascends peripheral nerves to CNS; near-100% fatality rate. - If patient comes into contact with rabid animal, give rabies IVIG + multiple courses of vaccine. - Qbank will focus on exact days/spacing to give vaccine. Waste of time/garbage.
Amoebic meningoencephalitis	<ul style="list-style-type: none"> - <i>Naegleria fowleri</i>; amoeba that lives in lakes, streams, hot springs that enters through the cribriform plate. - Causes rapid deterioration and death within days. - You’ll see a news article on this every 6 months or so about some “brain-eating amoeba” that killed person who swam in lake.
Eosinophilic meningoencephalitis	<ul style="list-style-type: none"> - <i>Angiostrongylus</i> (rat lung worm). - Consumption of raw slugs/snails. - Caused paralysis and death in an Australian teenager who ate raw garden slug after being dared by friends.

Cavernous sinus thrombosis
<ul style="list-style-type: none"> - Severe headache, diplopia, proptosis, and/or ophthalmoplegia in patient with recent sinus infection. - Bacterial infection can ascend the valveless facial veins to the cavernous sinus, leading to clotting of blood. - Usually <i>S. aureus</i>. - Tx = IV antibiotics + heparin. - CN VI palsy can occur with pathologies of the cavernous sinus.

Primary CNS lymphoma
<ul style="list-style-type: none"> - HY and underrated diagnosis for USMLE. - Causes ring-enhancing lesion on head CT that can be mistaken for Toxo. As discussed above, if AIDS patient has CD4 count <100 and is already on TMP-SMX, the Dx is primary CNS lymphoma, not Toxo. - Can be seen in non-AIDS patients who have immunosuppression due to other causes (i.e., organ transplant recipients on immunosuppressant meds; patients undergoing radio- and/or chemotherapy). - Can be caused by autoimmune diseases. For example, if they give you a 1-liner where they say, “44-year-old woman with SLE has ring-enhancing lesion on CT” → answer = CNS lymphoma, not Toxo. - Many autoimmune diseases (e.g., SLE, dermatomyositis, Hashimoto) ↑ the risk of non-Hodgkin lymphoma.

Encephalopathy	
- General term that refers to altered brain function (usually presenting as confusion) due to various causes.	
Hepatic	<ul style="list-style-type: none">- Seen in alcoholism due to hyperammonemia.- Classically occurs on USMLE when there is an ↑ in blood in the GI tract, such as following acute variceal bleed. Blood is broken down in the GIT into proteins that liberate amino acids, which are converted by gut bacteria into ammonia that is absorbed.

	<ul style="list-style-type: none"> - Lactulose is important drug for USMLE for treatment of hepatic encephalopathy. It is a sugar that is broken down by gut bacteria into acidic products. This leads to the conversion of ammonia into ammonium. The latter is ionic and not readily absorbed. The USMLE wants "acidification; ammonium" as the answer for what happens when we give lactulose. - Neomycin is another drug for hepatic encephalopathy. It is an aminoglycoside antibiotic that kills ammonia-producing gut bacteria.
Uremic	- Confusion in the setting of renal failure due to elevated blood urea nitrogen.
Metabolic	- Confusion due to electrolyte imbalances, hypoglycemia, and thyroid storm.
Toxic	- Mental status changes due to toxins. Reye syndrome and lead poisoning are HY.
Inflammatory	<ul style="list-style-type: none"> - Herpes encephalitis (infectious). <ul style="list-style-type: none"> - Encephalitis is infection of the substance of the brain, causing confusion (encephalopathy). - As discussed earlier, infection + confusion = encephalitis; infection + stiff neck and/or photophobia = meningitis. - Lupus cerebritis (autoimmune).
Anoxic	- Confusion caused by diminished oxygen delivery to the brain.

Neuropathic pain disorders	
Diabetic neuropathy	<ul style="list-style-type: none"> - Presents as pain, paresthesia, and/or numbness in diabetic. - USMLE likes TCAs (i.e., amitriptyline) or gabapentin as first-line for Tx. - Use nortriptyline in elderly if a TCA is given (fewer side-effects).
Herpetetic neuralgia	<ul style="list-style-type: none"> - Pain, burning, tingling experienced prior to, during, or after herpes or varicella (shingles) episode. - Acyclovir is used to treat the virus; gabapentin used classically for the pain.
Post-trauma	<ul style="list-style-type: none"> - Patients who have injuries resulting in nerve trauma can sustain chronic neuropathic pain. Treat with gabapentin or TCAs. - Trauma can result in complex regional pain syndrome, which is neuropathic pain that occurs as sequela of injury that is disproportionate to the injury itself.
Thalamic pain syndrome	<ul style="list-style-type: none"> - Damage to the thalamus due to a stroke that results in body pain, usually contralateral to the side of the infarction, occurring many months post-stroke. - The answer on USMLE for severe limb pain many months following a stroke.

TNR + Prion disorders	
Huntington	<ul style="list-style-type: none"> - Autosomal dominant CAG trinucleotide repeat (TNR) expansion on chromosome 4 resulting in neurodegeneration and choreoathetosis. - Chorea = fast, purposeless, jerky movements; athetosis = slow, writhing movements. - Anticipation = disorder occurs earlier and more severe with each successive generation; caused by expansion of the TNR repeat. - USMLE likes caudate nuclei as part of the brain that's fucked up.
Friedreich ataxia	<ul style="list-style-type: none"> - Autosomal recessive GAA TNR disorder. - Causes ataxia, kyphoscoliosis, cardiomyopathy, pes cavus (high-arched feet), hammer toes, and early-onset type II diabetes.
CJD	<ul style="list-style-type: none"> - Creutzfeldt-Jacob disease. - Prion disease; a prion is a misfolded protein that causes the misfolding of other proteins. - CJD is abnormally folded protein within the CNS ($\text{PrP}^{\text{C}} \rightarrow \text{PrP}^{\text{SC}}$), where the former is an α-helix that becomes a misfolded β-pleated sheet. Sounds absurdly pedantic, but it's known to be asked for whatever reason. - If the misfolded PrP^{SC} variant of the protein comes into contact with normal PrP^{C} variants, it causes them to misfold into additional PrP^{SC}, with the process functioning exponentially. - Presents as neurodegeneration over weeks to months + myoclonus.

	- The myoclonus is the highest yield detail, since you will sometimes see CJD as a distractor answer, where I'll say to the student, "The patient doesn't have myoclonus though."
--	---

Infective neuropathies	
Polio	<ul style="list-style-type: none"> - RNA virus that infects the anterior horns of the spinal cord and causes polio myelitis (inflammation of spinal cord). - Classically causes degeneration of motor neurons in one leg, leading to one leg much smaller than the other leg. - Highest yield points about Polio actually have zero to do with the infection and almost all to do with the vaccines. - Salk vaccine = Killed intramuscular. - Sabin vaccine = live-attenuated oral. - USMLE will ask what is a common feature of these vaccines that accounts for their efficacy? → answer = "neutralizing antibodies in the circulation." - Only the live-attenuated vaccine is capable of generating a CD8+ T-cell response and IgA secretion in the gut. - However, both the killed and oral are capable of generating IgG antibodies in the circulation. - If you're confused about the immuno, I talk about this stuff in my HY Immuno PDF.
PML	<ul style="list-style-type: none"> - Progressive multifocal leukoencephalopathy. - Caused by JC polyoma virus. - Presents as neurodegeneration over weeks to months in immunocompromised patient, i.e., AIDS patient with CD4 count <100, patients undergoing chemoradiotherapy, or those on immunosuppressant drugs. - USMLE wants you to know this condition is due to "reactivation of latent infection," which means the patient is infected at some point during life years ago, but the condition now manifests due to immunosuppression. "Acute infection in immunocompromised patient" is the wrong answer.
TSP	<ul style="list-style-type: none"> - Tropical spastic paraparesis. - Obscure neurologic condition caused by HTLV-1/2 (the same virus that causes mycosis fungoides and Sezary syndrome; if you are like wtf?, I discuss these in my HY Derm PDF). - Development of anti-neuronal antibodies that presents as neurodegeneration.
SSPE	<ul style="list-style-type: none"> - Subacute sclerosing panencephalitis. - Obscure condition characterized by cognitive decline and neuropathy due to reactivation of certain strains of measles in the CNS. - Will present as teenager experiencing cognitive decline + CSF analysis shows measles.

Toxin-induced neuropathies	
Botulism	<ul style="list-style-type: none"> - Causes flaccid paralysis. - Botulin toxin of <i>Clostridium botulinum</i> inhibits presynaptic SNARE protein, resulting in ↓ release of presynaptic acetylcholine, which is normally stimulatory at muscles. - Can present as floppy baby syndrome; can also cause cranial nerve palsies. - USMLE can be weird about the answer, where I've seen them write on an NBME exam something along the lines of "prevents acetylcholine from binding to its receptor" as the MOA of the toxin, even though this isn't technically the direct effect. - Acquired as spores in honey in infants under 1; acquired as pre-formed toxin from canned goods in anyone older. - NBME exam wants you to know that administering the toxin does not change the effect of strength of the effect of acetylcholine binding to its receptor. This is because the toxin isn't a competitive inhibitor + only ↓ endogenous ACh release; this has no impact on any ACh administered exogenously.
Tetanus	<ul style="list-style-type: none"> - Causes spastic paralysis.



	<ul style="list-style-type: none"> - Tetanus toxin of <i>Clostridium tetani</i> inhibits presynaptic SNARE protein, resulting in ↓ release of presynaptic neurotransmitters GABA and glycine, which are normally inhibitory. - Can present as opisthotonos (arched back) and trismus (lock-jaw). - Presents in two patients on USMLE: 1) neonate born at home whose umbilical cord was cut with a kitchen knife + tied with twine; 2) random dude who cut himself in back yard. - DTaP given at 2, 4, 6, months, then again at 15-18 months, then again at 4-6 years. - School-age kids require Tdap booster at 11-12 years, followed by Td booster every 10 years thereafter. - Pregnant women should get Tdap at 27-36 weeks to protect neonate from pertussis. <p>For cuts/wounds post-vaccine:</p> <ul style="list-style-type: none"> - 0-5 years post-vaccine: no Tx is necessary. - 6-9 years post-vaccine: if clean wound: no Tx; if dirty wound: give Td booster. - 10+ years post-vaccine: if clean wound: give Td booster; if dirty wound: IVIG + vaccine. - In other words, only ever give IVIG if it's a dirty wound + has been 10+ years.
Tetrodotoxin	<ul style="list-style-type: none"> - Toxin acquired by pufferfish. - Inhibits sodium channels; causes paralysis and death.
Ciguatera	<ul style="list-style-type: none"> - Toxin acquired by various meaty fish. - Prevents sodium channel closure. - The answer on USMLE for temperature dysesthesia ("hot feels cold; cold feels hot").

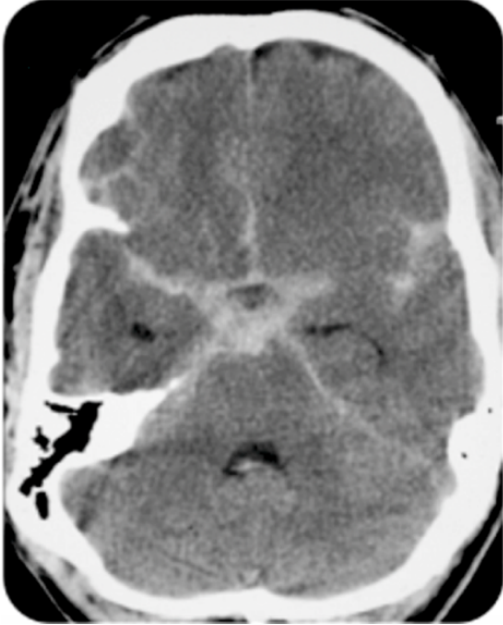

Narcolepsy

- Chronic sleep disorder affecting the brain's ability to regulate sleep-wake cycles normally.
- Characterized by excessive daytime sleepiness, sudden episodes of muscle weakness (cataplexy), sleep paralysis, and hallucinations. The latter tend to occur prior to sleep (hypnagogic) or upon waking up (hypnopompic).
- Thought to be due to deficiency of a neurotransmitter called orexin (aka hypocretin), which normally promotes wakefulness.
- Treatment is modafinil (dopamine reuptake inhibitor + promotes release of orexin from hypothalamus).

Brain bleeds

Epidural hematoma	<ul style="list-style-type: none"> - Rupture of middle meningeal artery (branch of external carotid); classically occurs following head trauma to the temple. - Lucid interval – i.e., patient loses consciousness briefly, followed by arousing and returning to normal (i.e., has a period of lucidity), then goes home thinking he/she is okay, then goes to sleep, then dies. - Bleed appears as lens (biconvex) shape; fast accumulating. - If low GCS, do "intubation + hyperventilation," <i>then</i> do craniotomy. If normal GCS, just do craniotomy. - Hyperventilation mechanism: decreased CO₂ → decreased cerebral perfusion → reduces intracranial pressure.
-------------------	---

	
Subdural hematoma	<ul style="list-style-type: none"> - Rupture of bridging (superior cerebral) veins. - No lucid interval (i.e., patient did not lose consciousness). - Crescent-shaped; can be slowly accumulating and heterogenous in appearance due to combination of dried + fresh blood. - Increased risk in elderly/dementia and alcoholics; answer in acceleration-deceleration injuries (shaken baby syndrome; motor vehicle accidents). - NBME wants craniotomy as the answer for Tx (no evidence for mere observation as the answer on any of the USMLE material). - If the patient has decreased Glasgow score, do "intubation + hyperventilation" as answer before craniotomy. 
Subarachnoid hemorrhage	<ul style="list-style-type: none"> - Rupture of anterior communicating artery (AcoM) or posterior communicating artery (PcoM) saccular/berry aneurysm. - AcoM > PcoM in terms of location. - Patient often reports "worst headache of his/her life." - Can present with stiff neck (meningism) the same way meningitis does, due to irritation of the meninges by the hemorrhage. This often confuses students and is a very HY detail. - PcoM aneurysm classically associated with ipsilateral blown pupil (mydriasis) due to CN III impingement. - HTN is most common risk factor in population and accounts for most cases. - Ehlers-Danlos and autosomal dominant polycystic kidney disease (ADPKD) are HY non-HTN-associated specific causes of saccular aneurysms.

	<ul style="list-style-type: none"> - A patient with HTN is still more likely to die from myocardial infarction than berry aneurysm (asked on NBME). But if patient has berry aneurysm, it is most likely from HTN. - Bleed appears like a “star fish” or “sand dollar.” Q can say there is blood visualized in the basal cisterns.  <ul style="list-style-type: none"> - Treatment is usually supportive. HTN must be controlled. Anticoagulants must be reversed (i.e., FFP for patients on warfarin). Nimodipine can prevent vasospasm and neurologic sequelae during convalescence.
Intracerebral hemorrhage	 <ul style="list-style-type: none"> - Rupture of Charcot-Bouchard microaneurysms within the lenticulostriate arteries in patients who have chronic HTN. - Can present on USMLE as a 1-2-line stem, without any image or patient info, where they just say, “X person has bleed + decorticate posturing; what’s the diagnosis?” → answer = intracerebral hemorrhage. - In other words, USMLE wants you to know intracerebral hemorrhage has high likelihood of causing brainstem compression.

	<ul style="list-style-type: none"> - Associated with Alzheimer (i.e., amyloid angiopathy, which presents in Alzheimer as recurrent hemorrhagic stroke). - Can be associated with brain cancer as well (e.g., glioblastoma multiforme).
Pituitary apoplexy	<ul style="list-style-type: none"> - Bleeding into the pituitary gland; can cause bitemporal hemianopsia. - USMLE wants you to know this can occur puerperium and also due to pituitary tumors. - 2CK form gives bitemporal hemianopsia in woman who just gave birth, where pituitary apoplexy is only answer listed that could cause this visual pattern.

Cushing reflex

- **Cushing reflex** is a triad seen with \uparrow ICP, where the patient will have: 1) HTN, 2) bradycardia, and 3) respiratory disturbance (classically \downarrow RR, but there's an NBME Q where they don't give RR as \downarrow).
- \uparrow ICP causes compression of intracerebral vessels \rightarrow chemoreceptors sense \downarrow oxygen delivery + \uparrow CO₂ \rightarrow this causes sympathetic activation and vasoconstriction of peripheral arterioles \rightarrow \uparrow BP \rightarrow \uparrow stretch of carotid sinus baroreceptors \rightarrow \uparrow CN IX afferent firing to solitary nucleus of medulla \rightarrow \uparrow CN X efferent firing to nodal tissue \rightarrow \downarrow HR.
- The \downarrow RR is due to \uparrow ICP causing compression of brainstem.
- NBME will give you a big 15-line paragraph with patient who's been in an accident + ask you for the reason for his or her HTN \rightarrow answer = "increased intracranial pressure."
- Don't confuse Cushing reflex with Cushing ulcer (completely unrelated), which is head trauma causing vagal outflow \rightarrow increased acid production + peptic ulcers.

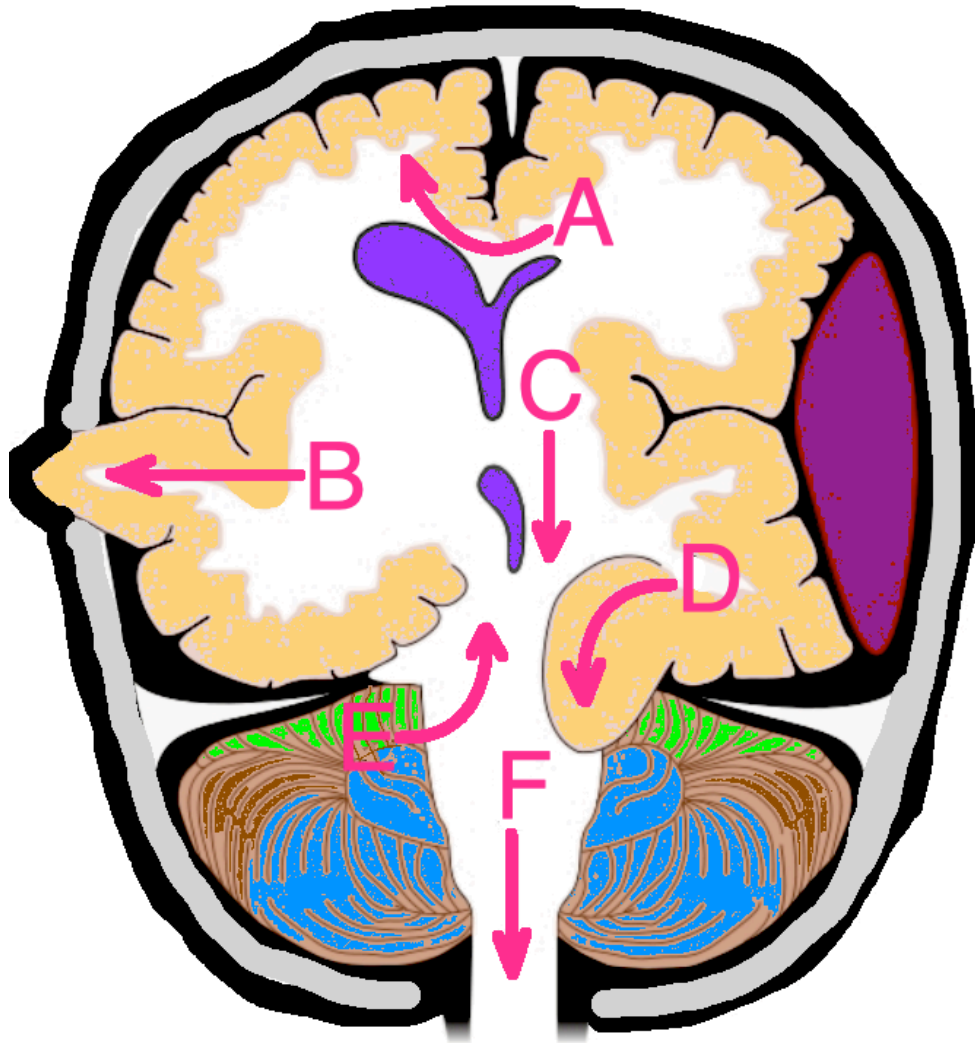
Glasgow coma scale (GCS)

Glasgow Coma Scale		
Response	Scale	Score
Eye Opening Response	Eyes open spontaneously	4 Points
	Eyes open to verbal command, speech, or shout	3 Points
	Eyes open to pain (not applied to face)	2 Points
	No eye opening	1 Point
Verbal Response	Oriented	5 Points
	Confused conversation, but able to answer questions	4 Points
	Inappropriate responses, words discernible	3 Points
	Incomprehensible sounds or speech	2 Points
	No verbal response	1 Point
Motor Response	Obeys commands for movement	6 Points
	Purposeful movement to painful stimulus	5 Points
	Withdraws from pain	4 Points
	Abnormal (spastic) flexion, decorticate posture	3 Points
	Extensor (rigid) response, decerebrate posture	2 Points
	No motor response	1 Point
Minor Brain Injury = 13-15 points; Moderate Brain Injury = 9-12 points; Severe Brain Injury = 3-8 points		

- It's to my observation across NBME exams (in particular 2CK Neuro CMS forms) that they will never ask you to formally calculate GCS score.
- What will occasionally surface in NBME Qs is "decorticate" or "decerebrate" posturing, where you have to know, "Oh that means GCS is low; patient has compromised brain function, possibly herniation / \uparrow intracranial pressure (ICP)."
- And as I mentioned earlier regarding suspected meningitis diagnostic workup, if GCS is not 15, then head CT should be done before LP.

Herniation types

- They ask this on a 2CK form, where they list all different types of brain herniations, where you're supposed to diagnose which one it is.



A	Cingulate (subfalcine)	<ul style="list-style-type: none"> - Doesn't usually produce specific Sx but can compromise blood flow in the anterior cerebral artery, which is necessary for contralateral motor/sensory to the leg. - The cingulate gyrus shifts under the falx cerebri.
B	Transcalvarial	<ul style="list-style-type: none"> - Symptoms vary based on the herniated tissue, ranging from no symptoms to seizures or focal neurological deficits. - Brain tissue extrudes through a skull defect.
C	Central transtentorial	<ul style="list-style-type: none"> - Decreased level of consciousness and bilateral motor abnormalities. - The diencephalic structures move downward through the tentorial notch.
D	Uncal	<ul style="list-style-type: none"> - Ipsilateral mydriasis + contralateral motor deficits. - Involves the medial temporal lobe (uncus) shifting into the tentorial notch. - The ipsilateral mydriasis is due to CN III compression. The contralateral motor deficits are due to compression of the cerebral peduncle.
E	Upward transtentorial	<ul style="list-style-type: none"> - Decreased level of consciousness; pupillary changes. - The diencephalic structures move upward through the tentorial notch.
F	Tonsillar	<ul style="list-style-type: none"> - Life-threatening respiratory and cardiovascular compromise. - Cerebellar tonsils move downward into the foramen magnum, compressing the brainstem. Can cause decerebrate or decorticate posturing.

Post-concussion syndrome

- A concussion is a type of traumatic brain injury caused by a blow to the head or by a sudden movement that results in the brain moving rapidly inside the skull. The rapid movement can cause brain cells to stretch and become damaged.
- Post-concussion syndrome (aka post-concussive disorder) comprises a range of symptoms that can persist for weeks, months, or even years after a concussion.
- Such symptoms include cognitive disturbance, memory loss, headache, and sensitivity to light or sound.
- USMLE will ask for the diagnosis straight-up on 2CK forms.

Base of skull fracture

- Fracture at base of the skull (you'd never have guessed it). Classic tetrad of signs is:
 - 1) Battle sign, which is bruising over the mastoid process behind the ear.
 - 2) Raccoon eyes, which refers to bilateral periorbital ecchymoses (bruising around both eyes).
 - 3) Otorrhea (CSF leaking out of the ear).
 - 4) Rhinorrhea (CSF leaking from the nose).
- Hemotympanum can also be seen, which is blood visualized behind the tympanic membrane.

CNS malignancy

- Can present with seizure and/or morning vomiting (a sign of \uparrow ICP).
- Can be described as ring-enhancing lesions (i.e., this descriptor is not limited to Toxo; it can also be tumors/metastases and abscesses).

Peds brain tumors

Pilocytic astrocytoma	<ul style="list-style-type: none"> - Most common brain tumor in kids. - Has solid (white) and cystic (black) components on imaging. - Not aggressive.
Medulloblastoma	<ul style="list-style-type: none"> - Aggressive brain tumor of cerebellum. - Can cause truncal ataxia if located at vermis, and ipsilateral limb ataxia if lateral.
Craniopharyngioma	<ul style="list-style-type: none"> - Most common pituitary tumor in children and teenagers. - Bitemporal hemianopsia (can occur with any pituitary lesion). - Embryo is that it originates from the "roof of the primitive oropharynx," or "roof of the primitive oral cavity." - Can calcify and contain cholesterol crystals; high rate of recurrence. - Don't confuse that embryo with "endoderm of foramen cecum," which refers to thyroglossal duct cyst.
Pinealoma	<ul style="list-style-type: none"> - Can cause vertical gaze palsy in kids (Parinaud syndrome).
Hamartomas	<ul style="list-style-type: none"> - The "tubers" in tuberous sclerosis are hamartomas, which are described as periventricular or cortical nodules on imaging.

Adult brain tumors

Glioblastoma multiforme	<ul style="list-style-type: none"> - Most common adult brain tumor; aggressive. - Aka "butterfly glioma," since it can cross through the corpus callosum. - Heterogenous in appearance due to areas of necrosis and hemorrhage. - USMLE wants you to know GM is a grade IV fibrillary astrocytoma.
Meningioma	<ul style="list-style-type: none"> - Benign tumor that grows from the meninges and appears to sit on top of the brain. - NBME Q floating around gives one that they describe as adjacent to falx cerebri. - <i>Can also occur within the spinal canal, overlying the spinal cord (on NBME).</i>
Schwannoma	<ul style="list-style-type: none"> - Arises from Schwann cells, which are responsible for myelinating peripheral nerves. - Vestibular schwannoma arises from CN VIII (vestibulocochlear nerve), often at the cerebellopontine junction, and can cause tinnitus and/or vertigo. - Can be idiopathic or as part of neurofibromatosis type II (NF2). - USMLE wants you to be able to identify its growth as causing sensorineural hearing loss (Rinne: AC > BC; Weber: lateralizes contralaterally).
Prolactinoma	<ul style="list-style-type: none"> - Most common pituitary tumor in adults.

	<ul style="list-style-type: none"> - Can cause amenorrhea in women and impotence in men. - Galactorrhea can occur in everyone. - I discuss other pituitary tumors and hormones in detail in the HY Endocrine PDF.
Optic glioma	<ul style="list-style-type: none"> - Seen in neurofibromatosis type I (NF1).
Oligodendroglioma	<ul style="list-style-type: none"> - Tumor of oligodendrocytes (the cells that normally myelinate CNS neurons). - Histo has fried-egg appearance and chicken-wire capillary pattern.
Ependymoma	<ul style="list-style-type: none"> - Tumor of ependymal cells, which normally produce CSF. - Rosenthal fibers on histo (eosinophilic corkscrew filaments).
Tumor of foramen magnum	<ul style="list-style-type: none"> - Can cause hypoglossal nerve (CN XII) palsy, leading to ipsilateral tongue deviation. - Shows up on a 2CK form. - So you should know that CN XII lesions occur from medial medullary syndrome as well as tumors of the foramen magnum.
Metastases	<ul style="list-style-type: none"> - Can be described as lesions at the grey-white junction. - Choriocarcinoma and lung cancer love to metastasize to brain.

Tic disorders	
Tourette	<ul style="list-style-type: none"> - Neurologic disorder characterized by repetitive, involuntary movements and vocalizations (i.e., tics). - Motor tics range from mere eye blinking, head jerking, or shoulder shrugging to more complex movements such as hopping, twirling, or even mimicking others' actions. - Vocal (phonic) tics include throat clearing, sniffing, or humming. More complex vocal tics can involve repeating words or phrases, or shouting inappropriate words (coprolalia). - Haloperidol and clozapine are two agents used to Tx that show up on NBME.
Provisional tic disorder	<ul style="list-style-type: none"> - In pediatrics it is normal for the kid to sometimes have a singular tic that lasts up to a year (e.g., unusual tongue or lip gesture). - There is very low chance of it progressing to chronic tic disorder / Tourette. - USMLE wants follow-up in 3-6 months as the next best step (i.e., observe).
PANDAS	<ul style="list-style-type: none"> - As mentioned earlier, there is an obscure condition called Pediatric Autoimmune Neuropsychiatric disorder Associated with Streptococci, where Group A Strep pharyngitis can cause a tic disorder, OCD, or ADHD in the weeks following infection. - USMLE will give you kid who had sore throat two weeks ago + now has a new-onset tic, ADHD, or OCD, and they will ask what will most likely diagnose etiology for the disorder → answer = "anti-streptolysin O titers."
Drug-induced	<ul style="list-style-type: none"> - Stimulants such as methylphenidate, amphetamines, and caffeine can cause tics. - Tardive dyskinesia due to anti-psychotics is considered a type of tic disorder.

Seizure terminology	
FOAS	<ul style="list-style-type: none"> - Focal-onset aware seizure (FOAS). - Formerly known as simple seizures. - No loss of consciousness (LoC).
FOIAS	<ul style="list-style-type: none"> - Focal-onset impaired awareness seizure (FOIAS). - Formerly known as complex seizures. - LoC. - This includes staring into space blankly, as with absence seizures (discussed below).
Partial	<ul style="list-style-type: none"> - One part of the brain is affected. - Simple partial = no LoC + only affects one part of brain. - Complex partial = LoC + only affects one part of brain.
Generalized-onset	<ul style="list-style-type: none"> - Formerly known as generalized. - Dumb changes in nomenclature. But I don't know what to tell you. - Involves both cerebral hemispheres.

Tonic-clonic	<ul style="list-style-type: none"> - Aka "grand mal" seizure; type of generalized seizure. It is characterized by two phases: - Tonic phase: lasts a few seconds; muscles stiffen and the patient falls to the ground and loses consciousness. - Clonic phase: rhythmic jerking movements of the limbs; usually lasts several minutes. - Following the seizure (i.e., during the postictal phase), the patient may be confused, drowsy, and have no recollection of the seizure. - Tongue biting/lacerations are a HY post-seizure finding. If the Q tells you explicitly that the tongue is normal in this setting, they are telling you it is not a seizure. - Tx for recurrent seizures are agents such as valproic acid, carbamazepine, and phenytoin. I discuss these later in this PDF in the pharm section. - There is a difficult NBME Q where they tell you a patient has twitching of one arm prior to falling to the ground and having a tonic-clonic seizure. The answer on the NBME form is "complex partial," not generalized tonic-clonic. This type of seizure is called FOIAS with secondary generalization, or complex partial with secondary generalization. - In other words, if a patient has focal neurologic signs preceding a tonic-clonic seizure, this indicates an origin in one location prior to spreading to other areas.
Status epilepticus	<ul style="list-style-type: none"> - The updated definition is a seizure lasting >5 minutes, or 2 seizures within 5 minutes. - Definition used to be a seizure lasting >30 minutes, or 2 seizures within 30 minutes. - First-line Tx is a benzo (IV lorazepam is usually 1st-line, but USMLE doesn't care). - If benzo doesn't work, phenytoin (or fosphenytoin) is next, followed by barbiturates. - In other words, for USMLE: benzo → phenytoin → barbiturate (e.g., phenobarbital).
Myoclonic	<ul style="list-style-type: none"> - A type of generalized seizure that causes muscle jerks lasting less than a second. - A succession of jerks can be seen over a short time period. - The patient will not have loss of consciousness. - Can present similarly to simple partial, despite the EEG showing generalized activity.
Febrile seizure	<ul style="list-style-type: none"> - Fever can precipitate idiopathic seizure in 2-4% of children ages 6 months - 5 years. - About a two-fold risk progression to epilepsy compared to general population. - Tx is with benzodiazepine. - Febrile seizures lasting longer than 10 minutes, seizures that are recurrent within 24 hours, or focal neurologic signs more significantly ↑ risk of progression to epilepsy.
Absence seizure	<ul style="list-style-type: none"> - Vignette will be a kid staring off into space in class for 30 seconds spacing out, sometimes with rapid blinking. - This is considered loss of consciousness. - EEG shows symmetric 3-Hz spike-and-wave discharges. - Tx is ethosuximide (thalamic calcium channel blocker).

Epilepsy disorders	
Temporal lobe epilepsy	<ul style="list-style-type: none"> - Most common epilepsy disorder. Originates at the medial temporal lobe. - Seizures are often preceded by visual auras, or warning signs. These can manifest as gustatory/olfactory sensations or déjà vu. - FOIAS are most common type, with or without secondary generalization. - For USMLE, pick "medial temporal lobe," or just "temporal lobe," if they ask for the origin of a seizure in the absence of any preceding neurologic findings.
West syndrome	<ul style="list-style-type: none"> - Aka infantile spasms; X-linked recessive. - Epilepsy syndrome in infants characterized by – you'd never guess it – spasms. - Causes an abnormal EEG pattern called hypsarrhythmia, which is chaotic pattern. - Leads to intellectual disability. - Treatment is with ACTH (obscure, but apparently ↑ endogenous cortisol, which can mitigate the progression).
Lennox-Gastaut	<ul style="list-style-type: none"> - Severe childhood-onset epilepsy characterized by near-daily seizures and cognitive decline (hyperoralemia is a sign of cognitive regression [babies put things in their mouths]).

	<ul style="list-style-type: none"> - Poor prognosis, with 5% mortality rate in childhood; 80-90% persistence of seizures into adulthood.
JME	<ul style="list-style-type: none"> - Juvenile myoclonic epilepsy. - Characterized by myoclonic jerks (usually hypnagogic and/or hypnopompic) that progress to tonic-clonic seizures after several months. - Age of onset is usually 10-16, but can also start in adulthood. - Tx is valproic acid.

Conditions misconstrued as seizures	
Adams-Stokes attack	<ul style="list-style-type: none"> - Idiopathic arrhythmia disorder in Peds that causes transient hypoxia to the brainstem, resulting in seizure-like episodes. - EEG does not show any seizure activity. - Q will give you kid with miscellaneous arrhythmia description + describe twitching that sounds like seizure → answer = Adams-Stokes attack.
Breath-holding spell	<ul style="list-style-type: none"> - They'll say 3-year-old was having a tantrum followed by falling on the floor + appearing blue. - Child will involuntarily stop breathing following a trigger – e.g., being upset, frightened, or experiencing pain. - The child often cries or becomes upset, exhales forcefully, stops breathing, then develops cyanosis, which can sometimes be followed by brief loss of consciousness and jerking (can be mistaken for seizure). - Shows up on NBME so you need to know it exists.
Syncope	<ul style="list-style-type: none"> - Just be aware that syncope in elderly (e.g., from aortic stenosis or atrial fibrillation) can sometimes cause twitching of muscles that accompanies fainting, where it resembles a seizure. - The muscular activity is due to hypoxia to the brain, similar to Adams-Stokes attack. - Shows up on an NBME form as elderly patient with cardiovascular Hx who has seizure-like episode. - Vignette might say there is no evidence of tongue-biting (meaning not a seizure).

HY Peds neuro conditions	
Spinal muscular atrophy	<ul style="list-style-type: none"> - Aka Werdnig-Hoffman syndrome. - Genetic disorder affecting anterior horns. - Presents with profound hypotonia, absent reflexes, and tongue fasciculations.
Cerebral palsy	<ul style="list-style-type: none"> - Motor dysfunction and intellectual disability of varying severity, posited to be due to intrapartum conditions such as hypoxia. - Will show up on USMLE as spastic paraparesis in a child who has "scissoring" of the legs.
Chiari 1	<ul style="list-style-type: none"> - Downward displacement of the cerebellar tonsils into the foramen magnum. - Usually teenager or young adult. - Presents with headaches and neck pain, but can also be asymptomatic.
Chiari 2	<ul style="list-style-type: none"> - Herniation of both the cerebellum and brainstem through the foramen magnum and is commonly associated with meningocele. - Presents as a child with dysphagia and motor dysfunction.
Dandy-walker	<ul style="list-style-type: none"> - Absent cerebellar vermis + cystic dilation of 4th ventricle.
Fetal alcohol syndrome	<ul style="list-style-type: none"> - Most common cause of mental retardation. - Heart/lung defects (defective neural crest migration). - Smooth, flat, and/or elongated philtrum. - Thin vermilion border (thin upper lip). - Widely spaced eyes (hypertelorism), midface hypoplasia, short nose.

Phenylketonuria	<ul style="list-style-type: none"> - Autosomal recessive; deficiency of phenylalanine hydroxylase (or rarely THB, which is cofactor for the enzyme), causing inability to convert phenylalanine into tyrosine. - Screened for on heel-prick test at birth, since failure to detect PKU will result in mental retardation. - Phenylalanine-deficient diet must be given. - Presents as child with “mousy” or “musty” body odor + appears lighter skin than siblings (can cause partial albinism, since tyrosine is normally converted into melanin, and tyrosine can’t be synthesized).
Maple syrup urine disease	<ul style="list-style-type: none"> - Autosomal recessive; deficiency of branched-chain ketoacid dehydrogenase. - Inability to breakdown leucine, isoleucine, and valine. - Causes a maple syrup-scent in the diapers from the urine. - Mental retardation and neurologic abnormalities if untreated.
Cretinism	<ul style="list-style-type: none"> - Aka congenital hypothyroidism. - Most common causes are iodine deficiency in the mother during pregnancy (worldwide) and fetal thyroid dysgenesis (western countries). - Leads to mental retardation (poor myelin sheath development), impaired bone growth, hypotonia, macroglossia, and protuberant abdomen (due to umbilical hernia; can be confused with kwashiorkor, which is protein-calorie malnutrition causing ascites). - Screened for at birth using the heel-prick test to prevent exacerbation.
Waardenburg syndrome	<ul style="list-style-type: none"> - Congenital sensorineural hearing loss + pigmentary changes of hair and skin. - Shows up on NBME as young child with “white forelock” of hair. - Answer = failure of neural crest migration.
Double cortex syndrome	<ul style="list-style-type: none"> - Obscure condition asked on USMLE students are hysterical about. - Genetic condition where neurons are unable to migrate outwardly to reach their destination in the cortex, resulting in two grey matter layers (cortex) instead of one. - Mechanism USMLE wants is “failure of radial migration.”
Rett syndrome	<ul style="list-style-type: none"> - Neurologic degeneration that occurs exclusively in female infants. - “Hand-wringing” or “hand-flapping” is buzzy finding. - Mental regression can present as putting objects in one’s mouth (something babies normally do).
Cri-du-Chat	<ul style="list-style-type: none"> - Deletion on short arm of chromosome 5. - Results in distinctive cat-like cry during infancy, which is the source of the syndrome’s name (French for “cry of the cat”). - Mental retardation, distinctive facial features, and microcephaly.
Friedreich ataxia	<ul style="list-style-type: none"> - As mentioned earlier, autosomal recessive GAA TNR disorder. - Causes ataxia, kyphoscoliosis, cardiomyopathy, pes cavus (high-arched feet), hammer toes, and early-onset type II diabetes.
Angelman	<ul style="list-style-type: none"> - “Happy puppet” – i.e., child presents with laughter. - Paternal imprinting → gene coming from dad is normally silenced; mom’s gene is supposed to be expressed but is deleted or mutated. - “Mom is not an angel” because mom’s gene is deleted. - Even if dad’s gene is healthy, since it is normally silenced, it will not be expressed. - Can also be caused by paternal uniparental disomy. Since the gene is normally paternally imprinted, if both alleles are inherited from dad, both will be silenced; disease occurs because there’s no maternal allele available to be expressed.
Prader-Willi	<ul style="list-style-type: none"> - Mental retardation + hyperphagia. - Maternal imprinting → gene coming from mom is normally silenced; dad’s gene is supposed to be expressed but is deleted or mutated (“Willi hates his dad” because dad’s gene is deleted). - Even if mom’s gene is healthy, since it is normally silenced, it will not be expressed. - Can also be caused by maternal uniparental disomy. Since the gene is normally maternally imprinted, if both alleles are inherited from mom, both will be silenced; disease occurs because there’s no paternal allele available to be expressed.

Rinne + Weber tests	
Rinne test	<ul style="list-style-type: none"> - A vibrating tuning fork is placed against the mastoid bone (bone conduction; BC). Once the patient can no longer hear it, it is removed from the bone and placed in front of the ear canal (air conduction; AC). - For both normal hearing and sensorineural hearing loss, AC > BC. - For conductive hearing loss, BC > AC.
Weber test	<ul style="list-style-type: none"> - A vibrating tuning fork is placed on the center of the forehead or top of the head, and the patient is asked if they hear the sound equally in both ears or if it's louder in one ear. - If it is louder in one ear, this is called "lateralization" to that ear.
Normal hearing	- Rinne shows air > bone conduction; Weber does not lateralize.
Conductive on left	- Rinne shows bone > air conduction; Weber lateralizes (is louder) to left.
Conductive on right	- Rinne shows bone > air conduction; Weber lateralizes to right.
Sensorineural on left	- Rinne shows air > bone conduction; Weber lateralizes to right.
Sensorineural on right	- Rinne shows air > bone conduction; Weber lateralizes to left.

Cholinergic concept review
<ul style="list-style-type: none"> - If an agent is cholinergic, it will cause DUMBBELSS signs/symptoms → Diarrhea, Urination, Miosis, Bradycardia, Bronchoconstriction, neuromuscular Excitation, Lacrimation, Salivation, Sweating. - If an agent is anti-cholinergic, it will cause the opposite of DUMBBELSS, or "anti-DUMBBELSS" → Constipation, Urinary retention, Mydriasis, Tachycardia, Bronchodilation (in reality, β_2 agonism, but not M antagonism, will bronchodilate), Skeletal muscle relaxation, Dry eye, Dry mouth, Anhydrosis. - The reason knowing this stuff is important is because TCAs (e.g., amitriptyline), antipsychotics, and 1st-generation H1 blockers (i.e., diphenhydramine, chlorpheniramine) have strong anti-cholinergic side-effects, which means they can cause "anti-DUMBBELSS" in any patient. In addition, anti-cholinergic effects promote delirium and confusion, especially in the elderly. - For example, old dude + high creatinine + on amitriptyline = post-renal azotemia due to a combo of BPH (which all old dudes have) and the TCA, which is anti-cholinergic. You want to take him off any anti-cholinergic meds he's on. Likewise, if you get a psych Q where a patient has confusion/delirium and one of his or her drugs is diphenhydramine, the answer might be, "discontinue anti-cholinergic medications." - Cholinergic agents either: 1) agonize cholinergic receptors directly, or 2) increase the potentiation of ACh binding to its receptors by inhibiting acetylcholinesterase (the enzyme that breaks down ACh), thereby increasing ACh within the synaptic cleft. - Almost all anti-cholinergic agents block cholinergic receptors directly.

Pro-cholinergic meds	
Muscarinic receptor agonists	
Bethanechol	<ul style="list-style-type: none"> - Stimulates detrusor muscle. - Used for overflow incontinence in diabetic patients with neurogenic (i.e., hypo-contractile) bladder.
Carbachol	<ul style="list-style-type: none"> - Constricts pupil and lowers intraocular pressure. - Used for glaucoma. - See my HY Ophthalmology PDF for more detail on that stuff.
Pilocarpine	<ul style="list-style-type: none"> - Constricts pupil and lowers intraocular pressure. - Powerful agent used for closed-angle glaucoma.
Methacholine	<ul style="list-style-type: none"> - Causes bronchoconstriction. - Used to help diagnose asthma. If administered to patient (not during acute attacks), spirometry will worsen and asthma symptoms may be replicated.

Acetylcholinesterase inhibitors	
Donepezil	<ul style="list-style-type: none"> - Increases acetylcholine available in synaptic cleft (i.e., pro-cholinergic). - Used 1st-line for Alzheimer disease. - Galantamine and rivastigmine have same MOA and use-case, but LY.
Edrophonium	<ul style="list-style-type: none"> - Aka Tensilon (the brand name). - Short-acting acetylcholinesterase inhibitor. - Administration to patients with myasthenia gravis causes marked improvement in symptoms and muscle function. - Administration to patients with Lambert-Eaton syndrome does not result in as marked improvement of symptoms.
Pyridostigmine	<ul style="list-style-type: none"> - Treatment for myasthenia gravis.
Physostigmine	<ul style="list-style-type: none"> - Antidote for Jimson weed poisoning (asked on NBME). - Jimson weed contains atropine-like compounds that are anti-cholinergic.
Neostigmine	<ul style="list-style-type: none"> - Used post-surgically to reverse the effects of neuromuscular blockade. - Toward the end of surgery, administration helps increase availability of ACh so that it can bind to its receptors and displace the nicotinic receptor antagonists used for neuromuscular paralysis.
Organophosphates	<ul style="list-style-type: none"> - Vignette will either be backpacker in his/her 20s picking fruit on a farm, or someone who drank fluid in a suicide attempt. - The phosphate group binds to acetylcholinesterase, inhibiting it. - NBME Q asks how toxicity could best be prevented → answer = “wearing gloves,” where “wearing mask” is wrong answer. So acquisition occurs mostly through skin. - USMLE wants atropine first, followed by pralidoxime as Tx (discussed below).

Anti-cholinergic meds	
Muscarinic receptor antagonists	
Atropine	<ul style="list-style-type: none"> - Classic textbook drug that blocks muscarinic receptors. - Can be used to increase heart rate during surgery. - Given as 1st-line Tx for organophosphate poisoning before pralidoxime. - Pralidoxime is a special anti-cholinergic that works by regenerating functional acetylcholinesterase by kicking out the phosphate group that inhibited it.
Benztropine	<ul style="list-style-type: none"> - Used for acute dystonia due to anti-psychotics. - In other words, if patient starts anti-psychotic and then within hours to days gets stiff neck (torticollis), muscle rigidity (without fever), and/or abnormal eye movements (oculogyric crisis), this is 1st-line Tx. - Muscle rigidity with fever, in contrast, suggest neuroleptic malignant syndrome.
Diphenhydramine	<ul style="list-style-type: none"> - 1st generation H1-blocker that has strong anti-cholinergic side-effects to the point that it is often just characterized straight-up as a primary anti-cholinergic med. - Can be used same as benztropine for acute dystonia (USMLE won't list both). - Can be used for motion sickness (anti-cholinergic effects treat motion sickness). If USMLE tells you it is used in this setting + they ask you antagonism of which receptor enables its anti-motion sickness effect, the answer is M3. The wrong answer is H2, since this refers to stomach acid secretion. Diphenhydramine is an H1 blocker, not H2. - Most Qs on USMLE regarding diphenhydramine revolve around you knowing it should be discontinued from a patient's regimen, rather than added.
Prochlorperazine	<ul style="list-style-type: none"> - Anti-psychotic used as an anti-nausea med. - Even though it is an D2-receptor antagonist, as I mentioned before, anti-psychotics have anti-cholinergic side-effects. In this case, the anti-muscarinic side-effects are actually a “good” thing since these treat nausea and motion sickness.
Ipratropium	<ul style="list-style-type: none"> - One of the 1st-line agents used for COPD (asked on 2CK NBME). - COPD patients can be started on either a muscarinic receptor antagonist, such as ipratropium, or a beta-2 agonist, such as olodaterol.

	- New literature gets pedantic about the duration (i.e., long- vs short-acting) anti-muscarinics and beta-2 agonists, but USMLE doesn't (i.e., some sources say tiotropium is recommended over ipratropium 1 st -line now, but I've had students come out of the exam saying ipratropium showed up, but that it didn't matter since it was the only drug listed that worked anyway).
Oxybutynin	- Used for urge incontinence.
Scopolamine	- Scopolamine patches are used for motion sickness (i.e., put it on the arm before getting on a boat or plane). This drug is an anti-cholinergic straight-up. - As mentioned above, oral diphenhydramine can also be used for motion sickness, but scopolamine is the classic treatment.
Hyoscyamine	- Used sometimes for irritable bowel syndrome.
Non-depolarizing nicotinic receptor antagonists	
Tubocurarine	- "Non-depolarizing" means the agent does not cause any action potentials. - NBME Q mentions a non-depolarizing agent used for neuromuscular blockade during surgery, and the answer is just "tubocurarine" straight-up.
Vecuronium	- Used for paralysis during surgery. - Cisatracurium and rocuronium are other important agents.
Depolarizing nicotinic receptor agonist (acts as antagonist)	
Succinylcholine	- Functions as antagonist due to desensitization of receptors. - Binds to nicotinic receptors and agonizes them, causing initial action potentials and muscle twitching (fasciculations), prior to desensitization and muscle paralysis. - Akin to leuprolide causing desensitization of GnRH receptors with continued binding, where despite being a GnRH receptor agonist, it acts functionally as an antagonist. - Can cause malignant hyperthermia (high fever + muscular rigidity; treat with dantrolene, which inhibits the ryanodine Ca ²⁺ channel).
Smoking cessation agents	
Bupropion	- Dopamine + norepinephrine reuptake inhibitor; has anti-depressant effects. - Also antagonizes nicotinic receptors, which disincentivizes smoking, since doing so won't produce rewarding effects. - Lowers seizure threshold. Don't give to patients with eating disorders (electrolyte abnormalities increase seizure risk). - Doesn't cause sexual side-effects, unlike SSRIs.
Varenicline	- Used for smoking cessation. - Partial agonist at nicotinic receptors, but since this effect is less than endogenous ACh, it functions like an antagonist.

Epilepsy/hypnotic agents	
- USMLE doesn't care about MOAs for these. They care about side-effects mostly, as per my observation.	
Valproic acid	- Blocks sodium channels and ↑ GABA. - Used as an alternative to lithium in Tx of bipolar disorder. - Causes neural tube defects in pregnancy due to interference with folate metabolism.
Carbamazepine	- Blocks sodium channels. - Generic anti-epileptic; also used as prophylaxis for trigeminal neuralgia. - Causes neural tube defects in pregnancy due to interference with folate metabolism. - Can cause aplastic anemia and SIADH.
Phenytoin	- Blocks sodium channels. - Generic anti-epileptic. - Causes neural tube defects in pregnancy due to interference with folate metabolism. - Can cause fetal hydrantoin syndrome (finger nail hypoplasia + abnormal facies). - Used for status epilepticus if benzo fails.
Ethosuximide	- Blocks thalamic calcium channels. Only anti-epileptic USMLE might ask MOA. - Used for absence seizures.
Benzodiazepines	- Diazepam, lorazepam, midazolam, chlordiazepoxide, etc.

	<ul style="list-style-type: none"> - Bind to GABA-A receptor, which ↑ frequency of Cl⁻ channel opening, thereby allowing Cl⁻ to flow into the neuron, hyperpolarizing it and inhibiting it (i.e., ↓ firing). - Hypnotic (induces sleep); anxiolytic (reduces anxiety); anti-convulsant. - Given 1st-line for status epilepticus. - Clonazepam used for insomnia/anxiety (shows up on NBME). - Used for stimulant intoxication (i.e., cocaine, amphetamine, PCP). - Used for specific phobia (e.g., fear of flying). - Used for social phobia 2nd-line if patient has asthma, since we don't give propranolol in this setting (asked on NBME). - Used for alcohol withdrawal (delirium tremens / alcoholic hallucinosis). - USMLE wants you to know that alcohol also binds to and activates GABA-A receptor, but at a different location from benzos. There's an NBME Q where you have to select the illustration of an alcohol molecule and benzo binding to the same receptor, but at different sites. - Can cause respiratory depression. - Treat overdose with flumazenil (antagonist of benzo receptor).
Barbiturates	<ul style="list-style-type: none"> - Phenobarbital, thiopental, etc. - Bind to GABA-A receptor; ↑ duration of chloride channel opening, making them more efficacious (and dangerous) than benzos. - Used for general anesthesia. - Used for unremitting status epilepticus if benzos and phenytoin fail.
Non-benzo hypnotics	<ul style="list-style-type: none"> - Zolpidem, zaleplon. - Activate GABA-A receptor, but bind to a different subunit from benzos. - Can cause addiction similar to benzos.
Magnesium	<ul style="list-style-type: none"> - Used for Tx and prevention of eclamptic seizures in pregnancy. - Given to pregnant women giving birth <32 weeks' gestation for neuroprotection for the fetus. - Used for torsades arrhythmia and digoxin toxicity.
Lamotrigine	<ul style="list-style-type: none"> - Blocks sodium channels. - General anti-epileptic. - Can cause Stevens-Johnson syndrome.

Drugs for neuropathic pain	
TCA's	<ul style="list-style-type: none"> - Prevent reuptake of both serotonin and norepinephrine. - Amitriptyline, nortriptyline, imipramine. - Neuro use-case is neuropathic pain, i.e., diabetic peripheral neuropathy. - Causes CCC → Coma, Convulsions, Cardiotoxicity (QT prolongation on ECG). - Have nasty anti-cholinergic side-effects (cognitive dysfunction and urinary retention, especially in elderly).
Gabapentin	<ul style="list-style-type: none"> - Blocks calcium channels, leading to neuroinhibition. - Used for neuropathic pain, e.g., diabetic peripheral neuropathy.

Headache drugs	
Migraine	<ul style="list-style-type: none"> - Abortive therapy: NSAIDs first, then sumatriptan (serotonin receptor agonist). - Prevention: propranolol (beta-blockade).
Cluster	<ul style="list-style-type: none"> - Abortive therapy: oxygen. - Prevention: verapamil (non-dihydropyridine calcium channel blocker).
Tension	<ul style="list-style-type: none"> - Rest + acetaminophen.
Trigeminal neuralgia	<ul style="list-style-type: none"> - Abortive: goes away on its own because episodes last maximum 30-60 seconds. - Prevention: carbamazepine (sodium channel blocker).

Parkinson drugs	
Carbidopa-levodopa	<ul style="list-style-type: none"> - Combo frequently used for Tx of Parkinson disease. - Levodopa crosses the BBB to be converted to dopamine centrally. However, levodopa is subject to fast metabolism when administered alone. The addition of carbidopa functions as a competitive inhibitor of breakdown enzymes, resulting in increased levodopa availability for passage across the BBB. Do not confuse this mechanism with direct COMT inhibitors (tolcapone, entacapone), which prevent breakdown of L-dopa. - Carbidopa-levodopa can cause psychosis if administered in too-high a dose. This is assessed on 2CK Psych forms, where if patient gets psychotic episodes following recent addition of C-L to regimen, or following an increase in dose, the answer is simply "decrease dose of carbidopa-levodopa." "Discontinue carbidopa-levodopa is the wrong answer."
D2 receptor agonists	<ul style="list-style-type: none"> - Ropinirole, pramipexole, cabergoline, pergolide, and bromocriptine. - Used for Parkinson disease management. - Bromocriptine classic agent used for prolactinoma (dopamine agonism ↓ prolactin). - Ropinirole + pramipexole classically show up as restless leg syndrome treatment following making sure the patient is iron replete. New literature suggests gabapentin is first-line over D2 agonists now for RLS, but USMLE won't play trivia. They will give patient with RLS + say, "In addition to ropinirole, what else could be added?" And gabapentin will be the only answer listed that works.
Amantadine	<ul style="list-style-type: none"> - Used for Parkinson disease. - Increases presynaptic release of dopamine.
Selegiline	<ul style="list-style-type: none"> - Used for Parkinson disease. - Inhibits monoamine oxidase B, which is an enzyme that preferentially breaks down dopamine. - Can cause serotonin syndrome, either alone, or in combo with drugs like St John Wort or SSRIs.

Alzheimer drugs	
Donepezil	<ul style="list-style-type: none"> - As mentioned earlier, this is a cholinesterase inhibitor used in Alzheimer. - Rivastigmine and galantamine you can be aware of and have same MOA, but are LY.
Memantine	<ul style="list-style-type: none"> - NMDA glutamate receptor antagonist. - Glutamate receptor activation normally causes Ca^{2+} to flow into the neuron, leading to depolarization and neuroexcitation. In other words, USMLE wants you to know glutamate receptor is a ligand-gated calcium channel (where glutamate is the ligand that activates the channel). Antagonism causes neuroinhibition.

Neurotoxic drugs	
Vincristine	<ul style="list-style-type: none"> - Prevents microtubule assembly; used as general chemotherapy. - USMLE can ask what drug inhibits and answer is just "tubulin." - Peripheral / autonomic neuropathy. - Answer shows up as "toxic neuropathy" on a 2CK Neuro CMS form.
Cisplatin	<ul style="list-style-type: none"> - Crosslinking agent used as general chemotherapy. - Causes neuro- and ototoxicity.
Aminoglycosides	<ul style="list-style-type: none"> - 30S ribosomal subunit inhibitors used for gram-negative rods. Highest yield use-case is in combination with vancomycin as empiric Tx for endocarditis. - Gentamicin, tobramycin, amikacin (latter sounds unusual but shows up on an NBME). - Cause ototoxicity (sensorineural hearing loss and/or vertigo). - Cause nephrotoxicity.
Loop diuretics	<ul style="list-style-type: none"> - Block the $1\text{Na}^+/1\text{K}^+/2\text{Cl}^-$ symporter on the apical membrane of the thick ascending limb. - Furosemide, ethacrynic acid, etc., can cause sensorineural hearing loss and/or vertigo.
Aspirin	<ul style="list-style-type: none"> - Irreversible cyclooxygenase 1 and 2 inhibitor.

	- Most common symptom is tinnitus (ear-ringing).
Quinidine	- 1a sodium channel blocker used occasionally as anti-arrhythmic. - Causes cinchonism, which means headache + tinnitus.
Digoxin	- Na^+/K^+ -ATPase inhibitor used for advanced heart failure. - Optic neuritis presenting as yellow wavy, "Vincent van Gogh vision."
Ethambutol	- Arabinosyl transferase inhibitor used for TB treatment. - Causes optic neuritis (visual changes of any kind, e.g., blurry vision, central scotoma, red-green color blindness).
Sildenafil	- Phosphodiesterase-5 inhibitor used for erectile enhancement (Viagra). - Can cause blue haze. Apparently this is due to its ability to also inhibit PDE-6 found in retinal receptors (holy shit). Tadalafil (Cialis) doesn't inhibit PDE-6 the same way, so this effect is more just with Viagra. - Step 3 wants you to know that pilots cannot take this within 3 hours of getting on an airplane due to possible blue haze. Unusual/obscure factoid, as if one would require a boner before getting in the cockpit, no pun intended.

IM Psych

Depressive disorders	
Major depressive disorder (MDD)	<ul style="list-style-type: none"> - At least 5 out of 9 SIGECAPS must be present for at least a 2-week period. S – Sleep disturbance (insomnia or hypersomnia). I – Interest loss. G – Guilt or feelings of worthlessness. E – Energy loss. C – Concentration problems. A – Appetite changes (usually causes weight loss, but sometimes weight gain). P – Psychomotor agitation (restlessness; slowed speech or movements). S – Suicidal ideation. - The symptoms must cause socio-occupational impairment and must not be attributed to a substance or another medication condition. - As far as NBME Qs go, I can say that USMLE doesn't actually give a fuck about fulfilling the 5/9 criteria. They'll give you an elderly male who's a bit quiet + teary-eyed + who's had weight loss, and the answer is just depression. Students get confused because they don't count 5/9, but as I said, USMLE doesn't care. - It's to my observation that <i>weight loss</i> is one of the most buzzy indicators in a psych vignette that MDD is likely the answer. - Terminal insomnia (patient wakes up too early in the morning) can be seen. - Can cause ↓ libido, but patient still has nocturnal erections (asked on NBME). - Can be caused by beta-blockers (propranolol); asked on NBME. - Tx is with drugs such as SSRIs, CBT, and occasionally ECT.
Depression due to a medical condition	<ul style="list-style-type: none"> - Hypothyroidism is important cause of low mood and apathy. - USMLE likes post-MI and cancer diagnoses as causes of depression. - Q might give guy who's had weight loss + teary-eyed post-MI; answer on an NBME form is just sertraline (an SSRI).
Atypical depression	<ul style="list-style-type: none"> - Hypersomnolence + hyperphagia in the setting of depression that is reactive / ameliorates when positive circumstances present themselves. - This latter aspect is called "mood reactivity," where positive events or experiences can significantly improve mood; this distinguishes atypical depression from other forms of depression, where mood usually remains persistently low regardless of external circumstances. - Tx = CBT, SSRIs, or monoamine oxidase inhibitors (MAOIs). - MAOIs are considered to be highly efficacious but are not usually used first-line because of serotonin syndrome risk (discussed later).
Pseudodementia	<ul style="list-style-type: none"> - Not actual dementia. This is depression that presents as cognitive decline, usually in elderly. - Patients with depression who have apathy will perform poorly on the MMSE. - The Q might say the patient is unable to draw a clockface, but when prompted, is able to finish it quickly. They might also say patient remembers 0 out of 3 objects after 5 minutes. - Look for obvious signs of depression, such as short, quiet answers, and low mood.

Dysthymia and cyclothymia	
Dysthymia	- At least 2 years of depressed mood without fulfilling MDD criteria.
Cyclothymia	- At least 2 years of oscillation between depressed mood and hypomania (discussed below).

Bipolar disorder I and II	
<ul style="list-style-type: none"> - DIGFAST is the mnemonic for remembering how mania and hypomania present: - D – Distractibility (easily distracted / not able to focus). - I – Impulsivity (e.g., shopping sprees, reckless driving). - G – Grandiosity (inflated self-esteem / having sense of special powers or gifts). - F – Flight of ideas (rapidly shifting thoughts/ideas, sometimes with lacking coherence). - A – Activity increase (goal-directed activity; sexual activity; psychomotor agitation). - S – Sleep deficit (decreased need for sleep). - T – Talkativeness (pressured speech; term means haphazard loquaciousness, sometimes without pausing). 	
Mania	<ul style="list-style-type: none"> - State of intensely elevated, expansive, or irritable mood, often with marked impairment in judgment. - Usually lasts longer than a week and causes socio-occupational dysfunction (i.e., the patient works as dentist and can't go to work / has problems at work). - Can sometimes cause psychotic features and require hospitalization. - ↑↑ risk of suicide.
Hypomania	<ul style="list-style-type: none"> - Usually lasts longer than 4 days and does not cause socio-occupational dysfunction (i.e., the Q says patient works as dentist + maintains the job no issues). - Does not cause psychotic features and does not require hospitalization.
Bipolar I	- Diagnosed if patient has at least one manic episode, with or without a depressive episode.
Bipolar II	<ul style="list-style-type: none"> - Diagnosed if patient has at least one hypomanic episode + at least one major depressive episode. The patient must have never had a full-blown manic episode. - The reason at least one major depressive episode is required for diagnosis is because a hypomanic episode might be part of cyclothymia, rather than bipolar II, if the patient has merely experienced depressed mood in the past without a full-blown depressive episode.
<ul style="list-style-type: none"> - Treatment on USMLE is lithium or valproic acid. - Lithium can cause nephrogenic DI, hypothyroidism, and tremor. It is also a teratogen (causes Ebstein anomaly). New 2CK NBME has lithium causing serotonin syndrome. Very unusual/odd, but asked. - Valproic acid causes neural tube defects (interference with folate metabolism), tremor, and hepatotoxicity. If the Q gives you increased LFTs + tremor, choose valproic acid over lithium. 	

Psychotic disorders	
Schizophrenia	<ul style="list-style-type: none"> - Four points for diagnosis. 1) At least 6 months in duration. 2) Two or more of the following: <ul style="list-style-type: none"> - Hallucinations (always auditory on USMLE; hearing voices that aren't there). - Delusions (false beliefs; can be "bizarre," which refers to stuff like demons, aliens, and "the lord"). - Disorganized speech (often nonsensical or muffled speech). - Disorganized or catatonic behavior. - Negative symptoms (flattened/blunted affect, anhedonia [inability to feel pleasure], diminished speech). 3) Must have socio-occupational dysfunction (i.e., significant impairment in work, interpersonal relationships, or self-care). 4) Not attributed to a mood disorder (i.e., depression or bipolar), substance use, or another medical condition.
Schizophreniform	- Same as schizophrenia but 1-6 months in duration.
Brief psychotic disorder	- Same as schizophrenia but <1 month in duration.

Commonly confused conditions	
<p>The diagram illustrates three conditions using a horizontal baseline and colored curves representing mood or psychotic states:</p> <ul style="list-style-type: none"> Schizoaffective: A blue baseline labeled "Baseline of psychosis". A green curve below the baseline is labeled "Spike of depression". A pink curve above the baseline is labeled "Spike of mania". Depression with psychotic features: A green baseline labeled "Baseline of depression". Two blue curves above the baseline are labeled "Spikes of psychosis". Bipolar with psychotic features: A pink baseline labeled "Baseline of bipolar". Two blue curves above the baseline are labeled "Spikes of psychosis". 	
Schizoaffective	<ul style="list-style-type: none"> - At least two weeks of psychosis without a mood disorder (i.e., neither depression nor mania/hypomania), followed by periods of time with simultaneous psychotic and mood disorder. - For example, the Q will say a college student has been hearing voices for the past 6 weeks + has been staying up all night for the past month (i.e., 4 weeks of mania or hypomania + at least 2 weeks of psychosis alone). - The name of the condition starts with "schizo," so you can remember that psychosis is the baseline of the disorder (i.e., what the patient will have as his/her underlying baseline). Then the mood disorder spikes on top of it.
Depression with psychotic features	<ul style="list-style-type: none"> - Depression, rather than psychosis, is the baseline. The patient will have periods of time in which he/she only experiences major depression without any type of psychosis. Then the psychosis periodically spikes on top of the depression.
Bipolar with psychotic features	<ul style="list-style-type: none"> - Bipolar is the baseline, where the patient will have periods of either depression or mania alone, followed by psychosis spiking on top of it. - If the patient has periods of mania alone followed by a simultaneous spike of psychosis, this makes the diagnosis easier. - If the patient has a period of depression alone followed by spiking psychosis, it can appear like depression with psychotic features, except the patient will <i>also</i> have a history of at least one manic episode in the past.

Delusion disorder
<ul style="list-style-type: none"> - One or more non-bizarre delusion, without other signs of psychosis. - By non-bizarre, as discussed earlier, this refers to potentially plausible scenarios (e.g., people at work are stealing from or trying to undermine you) that are not true, whereas bizarre on USMLE is anything that involves aliens, demons, the heavens, the lord, etc. - The person's behavior and thinking, apart from the delusion itself, tend to be normal. - Tx = CBT, anti-psychotics (e.g., risperidone), mood-stabilizers (lithium), and/or anti-depressants (SSRIs).

Anxiety disorders	
Generalized anxiety disorder (GAD)	<ul style="list-style-type: none"> - 6+ months of excessive and persistent worry about various aspects of life, often accompanied by physical symptoms like restlessness, fatigue, and muscle tension. - USMLE might give 40-year-old woman who is worried about many things (e.g., her son going to college, her work, her marriage, etc.) for 6+ months. - Patient can also have concurrent mood or psychotic disorder. In this case, the diagnosis becomes, e.g., "GAD with comorbid MDD." - Tx for GAD is CBT and SSRIs. - Buspirone (serotonin receptor agonist) can also be used.
Panic disorder	<ul style="list-style-type: none"> - Panic disorder is diagnosed if patient has 2 or more panic attacks + at least one month of worry about having more attacks. - A panic attack is an episode of intense fear that triggers severe physical reactions, even though there is no real danger or apparent cause. - USMLE will usually give patient with hyperventilation, where he/she feels like he/she is going to die or is having an MI. The USMLE is obsessed with making you think panic attack is cardiac. Don't get fooled. - Vignette can mention a mid-systolic click (mitral valve prolapse) + ask you the cause of the patient's symptoms → answer = panic disorder, not mitral valve prolapse. Student is confused because they say, "But wait, the patient has a mid-systolic click though." You're right. But the MVP itself isn't the cause of the patient's presentation. MVPs are common in the population and almost always asymptomatic. - Tx = breathing exercises to encourage the patient to stop hyperventilating. Breathing into a paper bag is wrong answer. Often times they won't have breathing exercises as an answer, where benzo is correct.
Social phobia	<ul style="list-style-type: none"> - Fear of being judged, negatively evaluated, or rejected in a social or performance scenario. Presents on USMLE as fear of public speaking. - USMLE wants beta-blocker (propranolol or atenolol) as 1st-line Tx. - If Q gives you an asthma patient, choose benzo. They make this distinction on NBME. - CBT for longer-term management.
Specific phobia	<ul style="list-style-type: none"> - Fear of a specific object or situation leading to significant distress or functional impairment. High-yield example on USMLE is fear of flying. - USMLE wants benzo for acute relief; CBT for longer-term.
Agoraphobia	<ul style="list-style-type: none"> - Fear of being in places or situations from which escape might be difficult or embarrassing, or where help might not be available if one were to have a panic attack. - This usually refers to crowded, open spaces.
Separation anxiety disorder	<ul style="list-style-type: none"> - Excessive distress with separation from home or major attachment figure. - Peaks at 12-18 months of age and usually subsides by 2-3 years, but children can still get this up into their teenage years. - USMLE can give a vignette of a child going to summer camp or school who gets stomach aches on arrival.
Selective mutism	<ul style="list-style-type: none"> - Disorder where patient fails to speak in certain situations, such as when confronted with new people, despite being able to speak in other situations.

PTSD vs Acute stress disorder	
PTSD	<ul style="list-style-type: none"> - Post-traumatic stress disorder; presents as at least 1 month of reliving a traumatic event, usually with flashbacks or nightmares about the event. - Treatment includes CBT and group therapy. - SSRIs if medication used.
Acute stress disorder	<ul style="list-style-type: none"> - Same as PTSD, but presenting for 3 days to <1 month since the traumatic event.

Adjustment disorder

- Socio-occupational dysfunction starting within 3 months of one specific stressor (i.e., a breakup, loss of job, death, illness).
- Usually lasts <6 months. If longer than 6 months, it is called chronic adjustment disorder.
- The key is the single stressor, whereas GAD is many, or no one specific, stressor.
- The patient cannot have any psychotic symptoms but can have a mood disorder, where we call it "adjustment disorder with depressed mood," or "adjustment disorder with anxious mood," etc. I've seen NBMEs, particularly on 2CK psych forms, write answers like this.
- First-line Tx is CBT and SSRIs.

Attention-deficit/hyperactivity disorder (ADHD)

- Inattentiveness (i.e., distractibility, not listening when spoken to) and/or hyperactivity (i.e., fidgeting, inability to remain seated or engage in activities quietly) *at home and at school*. The pattern of behavior must be consistent across venues and daily situations the child is immersed in.
- Tx = 1st-line is stimulant meds, such as methylphenidate (Ritalin). Other non-stimulant meds, such as atomoxetine can be attempted 2nd-line.
- External to meds, family therapy, behavioral skills training, and parenting skills training can be pursued.
- Teenagers or adults can undergo CBT.

Obsessive-compulsive disorder (OCD)

- Obsessions = Unwanted and intrusive thoughts, images, or urges that cause significant anxiety or distress.
- Example is constantly feeling the need to touch a doorknob correctly before opening the door.
- Compulsions = Repetitive behaviors a person performs in response to an obsession.
- Example is touching the doorknob repeatedly in order to make sure it is touched "correctly."
- OCD is persistent obsessions and/or compulsions causing the patient significant distress or interfering with the patient's socio-occupational functioning. The patient need not have both in order to be diagnosed – i.e., a patient can just have either obsessions or compulsions alone.
- A key point that distinguishes OCD from OCDP (obsessive-compulsive personality disorder, which I discuss below), is that OCD is ego-dystonic, whereas OCDP is ego-syntonic – meaning, in OCD, the patient doesn't like it / feels distressed; in OCDP, the patient is content / doesn't view anything as wrong.
- Tx = CBT. If drugs, use SSRI or clomipramine (a TCA). The latter shows up on 2CK Psych form and is a mini-factoid about OCD (i.e., you can use the TCA clomipramine to treat it).

Conduct vs oppositional defiant disorder

Oppositional defiant	<ul style="list-style-type: none"> - Argumentative and defiant behavior, often leading to problems at school with teachers and/or problems with grades. - The vignette can sound like normal teenage behavior, but the emphasis will be that there is impediment to social and/or scholastic progression. - Another key point is that there is no law-breaking. If the vignette mentions anything about crimes, then the USMLE wants conduct disorder instead.
Conduct disorder	<ul style="list-style-type: none"> - >6-month pattern of law-breaking starting age 17 or younger. - Vignette might give a teenager who engages in criminal behavior, such as killing a cat, destroying property, or engaging in theft. - USMLE won't necessarily present to you a pattern of ongoing behavior, but rather just a snapshot of a child + ask for the diagnosis – i.e., 14-year-old killed a cat; what's the most likely diagnosis → answer = conduct disorder (because what he did is a crime); oppositional defiant disorder is wrong answer.

Eating disorders	
Anorexia	<ul style="list-style-type: none"> - Intense preoccupation with maintaining low body weight and an intense fear of gaining weight. BMI must be low (i.e., <18.5) for diagnosis. - Purging can be seen (not limited to bulimia). - Vignette can give girl who runs 12 miles per day and barely eats. - USMLE likes metatarsal stress fractures due to decrease bone density. - The Q can ask what the patient is at risk for later in life → answer = osteoporosis (reduced adipose → reduced estrogen). - Amenorrhea in females can be seen but is no longer mandatory for diagnosis. USMLE wants “abnormal GnRH pulsation” as the mechanism for amenorrhea in anorexia, where LH and FSH are both decreased. This is called hypogonadotropic, or central, amenorrhea. - BMI <15 or overt malnutrition is indication for hospital admission. - Tx is CBT and/or SSRI. Mirtazapine is an α_2-antagonist that stimulates appetite and is used for patients with depression and anorexia. - Avoid bupropion in patients with eating disorders (lowers seizure threshold). - Most common cause of death is ventricular fibrillation due to hypokalemia. - Olanzapine can be used in theory (anti-psychotic that ↑ appetite).
Bulimia	<ul style="list-style-type: none"> - Binge eating followed by compensatory behaviors such as vomiting, excessive exercise, or the use of laxatives. - BMI is normal or increased (unlike anorexia, where it must be decreased). - Tx is CBT and/or SSRI.

Factitious disorders for IM	
Factitious thyrotoxicosis	<ul style="list-style-type: none"> - Injection of thyroid hormone. Aka surreptitious thyrotoxicosis. - USMLE vignette will usually make this an endocrine-type Q (see HY Endocrine PDF), where it need not be attached to the patient’s desire to seek medical care (i.e., the patient could just be attempting to lose weight), however some patients will inject as a means to acquire medical attention. - Q need not say patient is a pharmacist (students use that as crutch).
Factitious use of glycemic meds	<ul style="list-style-type: none"> - Use of insulin or hypoglycemic meds (e.g., sulfonylureas) to achieve hypoglycemia or weight loss. - USMLE will usually ask this in the setting of C-peptide levels (i.e., low C-peptide indicates exogenous insulin; high C-peptide means either secretagogue abuse like sulfonylureas, or insulinoma). - Some patients use these meds to achieve medical attention.

Sleep disorders for IM	
Narcolepsy	<ul style="list-style-type: none"> - Chronic sleep disorder affecting the brain’s ability to regulate sleep-wake cycles normally. - Characterized by excessive daytime sleepiness, sudden episodes of muscle weakness (cataplexy), sleep paralysis, and hallucinations. The latter tend to occur prior to sleep (hypnagogic) or upon waking up (hypnopompic). - Thought to be due to deficiency of a neurotransmitter called orexin (aka hypocretin), which normally promotes wakefulness. - Treatment is modafinil (dopamine reuptake inhibitor + promotes release of orexin from hypothalamus).
Sleep apnea	<ul style="list-style-type: none"> - Can be obstructive (i.e., usually from obesity) or central (i.e., brain-related). - Chronic fatigue and poor oxygenation can lead to dysthymia / depression. The answer on NBME is “mood disorder due to a medical condition.”

	<ul style="list-style-type: none"> - Polysomnography (sleep study) is what USMLE wants to diagnose. - When obstructive sleep apnea progresses to the point that the patient is a chronic CO₂ retainer with pulmonary hypertension and/or cor pulmonale, we call it obesity hypoventilation syndrome (Pickwickian syndrome). If you're confused about the cardio, go to the HY Cardio PDF.
Restless leg syndrome	<ul style="list-style-type: none"> - Idiopathic, irresistible urge to move legs while in bed/sleeping. - Most common cause is iron deficiency anemia. First step is checking the patient's serum iron and ferritin. - If iron studies are normal, gabapentin and D₂ agonists (ropinirole, pramipexole) can be used. - USMLE wants you to know that patients with RLS have increased risk of developing Parkinson disease, which makes sense since D₂ agonists help, indicating a potential problem with dopamine signaling or production in some patients.

Tic disorders	
Tourette	<ul style="list-style-type: none"> - Neurologic disorder characterized by repetitive, involuntary movements and vocalizations (i.e., tics). - Motor tics range from mere eye blinking, head jerking, or shoulder shrugging to more complex movements such as hopping, twirling, or even mimicking others' actions. - Vocal (phonic) tics include throat clearing, sniffing, or humming. More complex vocal tics can involve repeating words or phrases, or shouting inappropriate words (coprolalia). - Haloperidol (typical anti-psychotic; D₂ antagonist) and clonidine (α_2 agonist) are two agents used to Tx that show up on NBME.
Provisional tic disorder	<ul style="list-style-type: none"> - In pediatrics it is normal for the kid to sometimes have a singular tic that lasts up to a year (e.g., unusual tongue or lip gesture). - There is very low chance of it progressing to chronic tic disorder / Tourette. - USMLE wants follow-up in 3-6 months as the next best step (i.e., observe).
PANDAS	<ul style="list-style-type: none"> - Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococci, where Group A Strep pharyngitis can cause a tic disorder, OCD, or ADHD in the weeks following infection. - USMLE will give you kid who had sore throat two weeks ago + now has a new-onset tic, ADHD, or OCD, and they will ask what will most likely diagnose etiology for the disorder → answer = "anti-streptolysin O titers."
Drug-induced	<ul style="list-style-type: none"> - Stimulants such as methylphenidate, amphetamines, and caffeine can cause tics. - Tardive dyskinesia due to anti-psychotics is considered a type of tic disorder.

Trichotillomania
<ul style="list-style-type: none"> - Pulling out one's hair; can be anywhere (i.e., eyebrows, scalp, etc.). - Patient may sometimes also eat his/her hair, leading to gastric bezoar (asked on NBME exam). This is an undigestible mass that can lead to bowel obstruction.

Important child abuse findings
<ul style="list-style-type: none"> - Spiral fractures (rotational/twisting force applied to bone). - Posterior rib fractures (squeezing). - Circular burns (cigarettes). - Burns sparing flexor regions (from being dipped in hot water [child flexes limbs to ↓ exposed surface area]). - Retinal detachment / hemorrhages. - Subdural hematoma (shaken baby syndrome).

- **Avoidance of eye contact** (if they say Hx of meningitis, think instead neurosensory hearing loss).

Peds bladder/bowel control	
Enuresis	<ul style="list-style-type: none"> - Nocturnal enuresis (i.e., wetting the bed) is normal on occasion up through age 5. - First step in ↓ recurrence is behavioral science-type answers (i.e., ↓ stressors + ↑ time spent with child). Q might say child wets the bed after a sibling is diagnosed with ALL (i.e., stressor). - After behavioral-type answers, the next step is star chart (positive reinforcement), where the child receives a star on a chart every time he/she doesn't wet the bed, where after, e.g., 10 stars, he/she gets an extra dessert. - If star chart is not listed, enuresis alarm is the next best step (i.e., literally an alarm that detects moisture in a child's underwear, typically using a sensor, where if moisture is detected, indicating urination, the alarm sounds or vibrates child awake, thereby encouraging him or her to stop urinating and go to instead use the toilet). - Answers such as imipramine, desmopressin, and water deprivation are wrong on USMLE.
Encopresis	<ul style="list-style-type: none"> - Shitting your pants. Normal on occasion up through age 5.

Psychosomatic disorders for IM	
Irritable bowel syndrome (IBS)	<ul style="list-style-type: none"> - Don't confuse with inflammatory bowel disease (IBD). - IBS is psychosomatic (i.e., psych-related) condition. - Classic vignette will be a woman 20s-40s with stress factors who usually has alternating diarrhea / constipation; can also present as bloating or cramping. - Key detail is that symptoms are relieved with bowel motions. - NBME assesses "smooth muscle hypersensitivity" as the answer for the mechanism for IBS. - Treatment for diarrhea-predominant IBS is loperamide, which is an opioid that causes constipation. USMLE will give vignette of IBS with diarrhea, and then the answer is just "mu-opioid receptor agonist."
Chronic interstitial cystitis	<ul style="list-style-type: none"> - Not an infection. - This is >6 weeks of suprapubic tenderness + dysuria (pain with urination) that is unexplained, where laboratory and urinary findings are negative. - They can mention anterior vaginal wall pain (bladder is anterior to vagina). - USMLE wants you to know you don't treat. Steroids are wrong answer. "Treatment" is standard placating placebo nonsense such as "education," "self-care" and "physiotherapy."
Fibromyalgia	<ul style="list-style-type: none"> - This is a psych condition, not an actual muscle disorder, but is often confused with polymyositis and polymyalgia rheumatica (see HY Anatomy/MSK PDF). - Labs will be normal. ESR will not be elevated. Patient will not have fever. - Will be described as woman 20s-50s with multiple (and often symmetric) muscle tenderness points. - Treatment is usually SNRIs or TCAs. USMLE can write this as "anti-depressant therapy." This confuses students ("But she doesn't have depression though.") → Right. But SNRIs and TCAs are still anti-depressant medication.

Delirium
<ul style="list-style-type: none"> - Acute disturbance in attention and cognition, usually over hours to days. - Most commonly presents as hyperactive delirium, which is where the patient appears confused, restless, agitated, and combative. - Can also present as hypoactive delirium, where the patient is mute, lethargic, or slow to respond to stimuli. - Important causes are infection, electrolyte disturbance (e.g., hypercalcemic crisis), medications (especially first-gen H1 blockers like diphenhydramine), and metabolic causes (e.g., hypercarbia in COPD exacerbation).

Hypercalcemic crisis	<ul style="list-style-type: none"> - Refers to cognitive dysfunction / a delirium-like state in the setting of severe hypercalcemia, often due to malignancy or primary hyperparathyroidism. - I've also seen this once in a patient on a thiazide (can cause hypercalcemia). - USMLE wants you to know that high calcium, as well as any sodium disturbance, can cause delirium. - First step on USMLE for Tx of hypercalcemia is normal saline. - After normal saline, USMLE wants bisphosphonate therapy (I've seen pamidronate listed on NBME). - I've never seen calcitonin or loop diuretics as correct answers for hypercalcemia Tx. They're always wrong.
Medication-induced delirium	
Reye syndrome	<ul style="list-style-type: none"> - As discussed earlier, acute encephalopathy and hepatic dysfunction caused by giving aspirin in the setting of a viral illness and/or fever. - Aspirin should be avoided under age 12, and some sources say avoid in teens for that matter. - Mechanism is obscure and thought to be related to impairment of β-oxidation.
Anti-cholinergic delirium	<ul style="list-style-type: none"> - Anti-cholinergic medications can cause confusion and a delirium-like presentation. Children have \uparrow susceptibility. - Q can mention a kid was given an over-the-counter medication and now has low-grade fever and confusion. - Details such as flushed, dry, warm skin, or enlarged pupils, suggest anti-cholinergic delirium over Reye. - Can be confused with Reye syndrome if they just say "over-the-counter" med. - 1st-gen H1-blockers (i.e., diphenhydramine) are notoriously anti-cholinergic.
Dextromethorphan	<ul style="list-style-type: none"> - Can cause delirium and psychosis in children when taken in excessive amounts. - An opioid that is an anti-tussive (cough suppressant).
Alcohol withdrawal	
Alcoholic hallucinosis	<ul style="list-style-type: none"> - Presents 12-48 hours after the last drink. - Patient can have hallucinations, usually tactile (i.e., bugs crawling on skin) or visual (bugs crawling up wall). - Treat with benzo + thiamine.
Delirium tremens	<ul style="list-style-type: none"> - Presents 2-4 days following last drink. - Patient will have tremulousness, tachycardia, diaphoresis, and restlessness. - Seizures can also sometimes occur. - USMLE-favorite vignette is 40s male who gets tremulousness and tachycardia while in hospital 2ish days after surgery. Answer is just benzo. - Can also show up on NBME as a guy who goes from drinking 12 beers a day to suddenly only 2 beers a day. - Treat with benzo + thiamine.

Drug abuse	
Glue	<ul style="list-style-type: none"> - Ataxia + cognitive decline in teenager. - Will sound a bit like alcohol abuse but the effects of alcohol don't occur so young.
Paint	<ul style="list-style-type: none"> - Cognitive decline. - Q can say teenager is seen with gold or silver coloration around the nose/mouth.
Butane (inhalant)	<ul style="list-style-type: none"> - Cognitive decline. - Classically inhaling computer cleaner (dusters) or whipped cream bottles. - Q will say high schooler found on floor in school bathroom + is brought into ED sluggish + pupils and vitals all normal \rightarrow answer = butane.
Caffeine	<ul style="list-style-type: none"> - Most common drug addiction in the world. - Adenosine accumulates in the brain throughout the day and causes sense of fatigue. - Caffeine blocks adenosine receptors, promoting sense of wakefulness. - Intoxication can cause sense of over-stimulation, panic, and palpitations.

	<ul style="list-style-type: none"> - Withdrawal can cause headache, sense of depression, fatigue, anxiety (i.e., sense of worry/doom), and inability to concentrate.
Smoking/vaping	<ul style="list-style-type: none"> - Nicotine can promote sense of euphoria. - Withdrawal can cause many symptoms, including anxiety, depression, difficulty concentrating, and weight gain due to increased appetite.
Marijuana	<ul style="list-style-type: none"> - Injection (redness) of conjunctivae + dry mouth. - ↑ risk of developing psychosis and schizophrenia.
Cocaine	<ul style="list-style-type: none"> - Mydriasis, tachycardia. - High BP causing aortic dissection; can cause chest pain (coronary vasospasm). - Abruptio placentae if pregnant teens. - Give benzo if acutely intoxicated + observe in emergency.
Amphetamine	<ul style="list-style-type: none"> - Mydriasis, agitation, insomnia / staying up all night. - Can cause tactile hallucinations. - Give benzo if acutely intoxicated + observe in emergency.
PCP	<ul style="list-style-type: none"> - Bellicosity / pugnacity (if you're ESL, those mean wanting to fight + aggressive). - Nystagmus +/- mydriasis. - One 2CK NBME Q gives mutism + constricted pupils for PCP + nothing about pugnacity, so just be aware this presentation is rare but possible. - Give benzo if acutely intoxicated + observe in emergency.
MDMA (ecstasy)	<ul style="list-style-type: none"> - Euphoria, heightened sensory perception, low-grade fever, bruxism (teeth grinding). - An NBME Q floating around gives increased creatine kinase, so this is also possible. - Give benzo if acutely intoxicated + observe in emergency.
LSD (acid)	<ul style="list-style-type: none"> - Visual hallucinations. - Give benzo if acutely intoxicated + observe in emergency.
MPTP	<ul style="list-style-type: none"> - Synthetic heroin. - Causes Parkinsonism. - Shows up on a 2CK form, so if you think it's weird, take it up with NBME, not me.
Heroin/opioids	<ul style="list-style-type: none"> - E.g., oxycodone or dextromethorphan. - Respiratory depression + constricted pupils + constipation. - Naloxone (opioid receptor antagonist) for acute toxicity. - Methadone (opioid receptor agonist) to ↓ relapses.
Benzos	<ul style="list-style-type: none"> - E.g., diazepam. - Respiratory depression. - Flumazenil to treat acute toxicity (benzodiazepine receptor antagonist).
Barbiturates	<ul style="list-style-type: none"> - Respiratory depression. - Q will say naloxone and flumazenil had no effect, so you eliminate to get to barbiturates.
Acetaminophen	<ul style="list-style-type: none"> - Fulminant liver failure. - Give activated charcoal if ingested within 1-2 hours. - N-acetylcysteine must be given after to regenerate reduced glutathione to prevent liver damage from NAPQI (acetaminophen metabolite).
Aspirin	<ul style="list-style-type: none"> - Tinnitus + mixed metabolic acidosis-respiratory alkalosis. - Give sodium bicarb to treat (↑ excretion through urinary alkalization).
TCAs	<ul style="list-style-type: none"> - E.g., amitriptyline. - CCCs (coma, convulsions, cardiotoxicity). - ECG changes seen frequently in vignettes. For example, you'll get a big vague paragraph about some drug overdose + they say in last line QT is prolonged → answer = the TCA. Then you remind student about cardiotoxicity and they're like Oh yeah. - Anti-cholinergic effects (i.e., delirium + hot, red, dry patient).

Depression meds	
SSRIs	<ul style="list-style-type: none"> - Selective-serotonin reuptake inhibitors. - Fluoxetine, escitalopram, sertraline, etc. - Cause sexual dysfunction (anorgasmia) and sleep disturbance. - The fact that they cause anorgasmia actually makes them the Tx for premature ejaculation. - Do not combine with drugs such as monoamine oxidase inhibitors or St John wort, as this can cause serotonin syndrome (discussed below). - There are unique side-effects of various SSRIs – e.g., sertraline is more likely to cause diarrhea; fluoxetine has a stimulating effect and is more likely to cause insomnia; citalopram can prolong QT interval at higher doses. But USMLE doesn't give a fuck. - Used for a variety of psych conditions external to depression, e.g., fibromyalgia, OCD, etc. - It can take 4-6 weeks for an SSRI to achieve desired effect. If after this time point the drug isn't working, the first step is increasing the dose. If this doesn't work, the next step is switching to a different SSRI, followed by switching to a different class agent.
SNRIs	<ul style="list-style-type: none"> - Serotonin and norepinephrine reuptake inhibitors. - Desvenlafaxine, duloxetine, etc. - Can increase blood pressure at higher doses.
TCAs	<ul style="list-style-type: none"> - Block reuptake of both serotonin and norepinephrine. - Amitriptyline, nortriptyline, clomipramine, doxepin, etc. - High-yield on USMLE as 1st-line for diabetic neuropathic pain; can also be used for neuropathic pain in general (e.g., from trauma). Gabapentin is otherwise frequently used. - Have nasty anti-cholinergic side-effects (anti-DUMBELSS; see HY Neuro PDF for discussion of anti-cholinergic vs pro-cholinergic effects if you're confused). - Three HY anti-cholinergic side-effect vignettes are <ol style="list-style-type: none"> 1) palpable suprapubic mass in an older male → full bladder as a result of anti-cholinergic med + BPH. 2) Hot, red, dry patient (as a result of anhidrosis). 3) Confusion + dilated pupils (anti-cholinergic delirium + mydriasis). - Coma, convulsions, cardiotoxicity. - Sometimes the Q can just mention prolonged QT interval in patient on an anti-depressant, and the answer is the TCA, since they're cardiotoxic. - If elderly, use nortriptyline, since ↓ BBB penetration and anti-cholinergic side-effects. - TCAs, such as imipramine, for nocturnal enuresis are wrong on USMLE. - Doxepin is asked on 2CK Psych form, where the Q rides on you knowing it's a TCA to get it right (i.e., the only drug listed that causes anti-cholinergic effects). I mention this because students get the Q wrong and then are like wtf is doxepin.
MAOIs	<ul style="list-style-type: none"> - Monoamine oxidase inhibitors. - Phenelzine, tranylcypromine. - Avoided 1st-line overwhelming majority of the time because of ↑ risk of serotonin syndrome. This can be in isolation, but also when commenced too soon following discontinuation of SSRI. - Selegiline is MAO-B inhibitor used for Parkinson disease. Answer on NBME where they ask which Parkinson med caused serotonin syndrome in a patient.
Bupropion	<ul style="list-style-type: none"> - Dopamine + norepinephrine reuptake inhibitor; has anti-depressant effects. - Also antagonizes nicotinic receptors, which disincentivizes smoking, since doing so won't produce rewarding effects. - Lowers seizure threshold. Don't give to patients with eating disorders (electrolyte abnormalities increase seizure risk). - Doesn't cause sexual side-effects, unlike SSRIs.
Mirtazapine	<ul style="list-style-type: none"> - α_2-antagonist; stimulates appetite; used for patients with depression and anorexia.
Trazodone	<ul style="list-style-type: none"> - Serotonin antagonist and reuptake inhibitor (SARI). - Used for depression, but is frequently used for insomnia due to strong sedative effects. - Can cause serotonin syndrome.

Serotonin syndrome

- Flushing, tachycardia, diarrhea following drug-drug interactions (i.e., MAOI + SSRI; SSRI + St John wort) or high-risk drugs in isolation (e.g., MAOI, trazodone, lithium). Lithium sounds unusual, but on new 2CK NBME.
- Can cause high fever, i.e., 105F+.
- Diagnose with urinary 5-hydroxyindole acetic acid (5-HIAA).
- Can be treated with cyproheptadine (blocks serotonin receptors).
- Often confused with carcinoid syndrome, which is due to carcinoid tumors (serotonin-secreting tumors) of the lung, small bowel, or appendix. Carcinoid syndrome isn't due to drugs. Additionally, it can cause tricuspid vegetations, whereas serotonin syndrome does not. It is still diagnosed with urinary 5-HIAA.

Anti-psychotic meds

- Categorized as typical (antagonize D2 receptors) or atypical (antagonize mostly D2 receptors, but also have additional binding effects at other receptors such as D4 or serotonin).
- HY Typical: Haloperidol, Chlorpromazine, Prochlorperazine, Thioridazine.
- HY Atypicals: Olanzapine, Clozapine, Quetiapine, Risperidone, Aripiprazole, Ziprasidone – i.e., Old Closets Quietly Whisper (Risper) from A to Z.
- All anti-psychotics can cause extra-pyramidal side-effects (EPS), anti-cholinergic side-effects, neuroleptic malignant syndrome (NMS), QT prolongation, and hyperprolactinemia (D2 agonism normally inhibits prolactin). I discuss side-effects in more detail below.
- Typical are older and more known for causing these effects. As a result, atypicals are usually the preferred first-line agents for schizophrenia and psychotic disorders.
- Typical like haloperidol are still occasionally used acutely for violent delirium, Tourette, or psychosis patients who have poor medication compliance. A 2CK form wants haloperidol decanoate as the answer for what's good to use for schizophrenia patient with poor compliance.
- Prochlorperazine can be used as an anti-nausea medication despite being a typical anti-psychotic.
- Clozapine can cause neutropenia (agranulocytosis). This is exceedingly HY.
- Olanzapine and clozapine can worsen obesity. Aripiprazole or ziprasidone are better for high-BMI patients.
- Chlorpromazine can cause Corneal deposits. Thioridazine can cause retinal deposits.

Extrapyramidal side-effects

- The name for the movement disorders associated with anti-psychotic use.
- "Rule of 4s" → After a patient is started on an antipsychotic, a general trend is seen in terms of the onset of particular symptoms. The time frame is not strict/rigid; use it as a general trend – i.e., acute dystonia wouldn't just start at 4 months; tardive dyskinesia wouldn't occur as early as 2 weeks.
- Acute dystonia at 4 hours → torticollis, oculogyric crisis, muscle rigidity without fever.
 - Torticollis = stiff / crooked neck.
 - Oculogyric crisis = weird eye movements (don't confuse with tongue movements of tardive dyskinesia).
 - Muscle rigidity without fever = acute dystonia. Muscle rigidity with fever = neuroleptic malignant syndrome.
 - Treat acute dystonia with benztropine or trihexyphenidyl (muscarinic receptor antagonists, which decrease muscle tone) or a 1st generation H1 blocker (diphenhydramine or chlorpheniramine). The latter have nasty anti-cholinergic (anti-muscarinic) side-effects that are *actually what we want* when we're treating acute dystonia. Maybe 2/3 of acute dystonia Tx Qs will have benztropine as the answer; ~1/3 will have one of the 1st gen H1 blockers as correct.
- Akathisia at 4 days → restlessness.
 - Treat with propranolol (beta-blockade).
- Parkinsonism at 4 weeks → akinesia / bradykinesia.
 - Treat with amantadine.
- Tardive dyskinesia at 4 months → abnormal facial movements (notably tongue).
 - Risk is greater with typicals compared to atypicals, but TD can be seen in the latter on NBME.
 - Treatment is stop the typical and give an atypical.

- Couple of weird Psych NBME Qs on this:
- Patient on *atypical* + gets TD; Tx? → stop the atypical and give another atypical. (Just stop the drug and switch to yet another atypical.)
- Patient on typical for 15 years and has no problems whatsoever (i.e., does not have TD); patient asks the psychiatrist what can be done to decrease his risk of developing TD; the correct answer is "stop the typical and give an atypical"; wrong answer is "maintain current drug regimen."
- Apparently even if the patient has been on a typical long term without an issue, switching to an atypical *still* confers a reduction of risk of TD.
- Metoclopramide (D2 antagonist used as anti-emetic / pro-kinetic) can also cause EPS side-effects and prolong QT interval, same as the anti-psychotics. There is 2CK Psych Q where they give Parkinsonism in patient on metoclopramide, and the next best step is "discontinue metoclopramide."

Neuroleptic malignant syndrome (NMS)

- Muscle rigidity and fever following commencement of anti-psychotic.
- The fever will usually be 103+ F, as per my observation on NBME exams. This is because mere anti-cholinergic side-effects can sometimes give low-grade fever (i.e., hot, red, dry patient).
- Mechanism for NMS is: the ryanodine channel, which allows calcium to move from the sarcoplasmic reticulum into the cytosol, gets stuck open, so ↑ calcium moves into the cytoplasm. The cell then needs to use a lot of ATP to pump the calcium back into the sarcoplasmic reticulum. This generates heat → fever.
- This mechanism for NMS secondary to anti-psychotic administration is the same as malignant hyperthermia (MH) due to succinylcholine (nicotinic neuromuscular blocking agent used during surgery).
- Tx is **dantrolene**, which closes the ryanodine channel.
- NBME will sometimes give vignette of NMS or MH, and then the answer for Tx is "decreases sarcoplasmic calcium release."
- In theory, bromocriptine (D2 agonist) can be used in the setting of NMS only as an alternative to dantrolene, but I haven't seen NBME assess this. This is more a pedantic Q students will ask sometimes.

Opioids for USMLE

- Mu (μ) and kappa (κ) are most well-studied, although delta (δ) and NOP forms exist.
- Mu agonism is responsible for most of the classic effects of opioids – i.e., analgesia, euphoria, respiratory depression, and dependence. Agonism results in inhibition of neuronal firing and neurotransmitter release via opening of K⁺ channels and closing of Ca²⁺ channels.
- Kappa has analgesic effects but can also produce dysphoria.
- Opioids can cause respiratory depression, miosis, and constipation.
- Opioid withdrawal can cause flu-like symptoms, irritability, piloerection, and yawning.

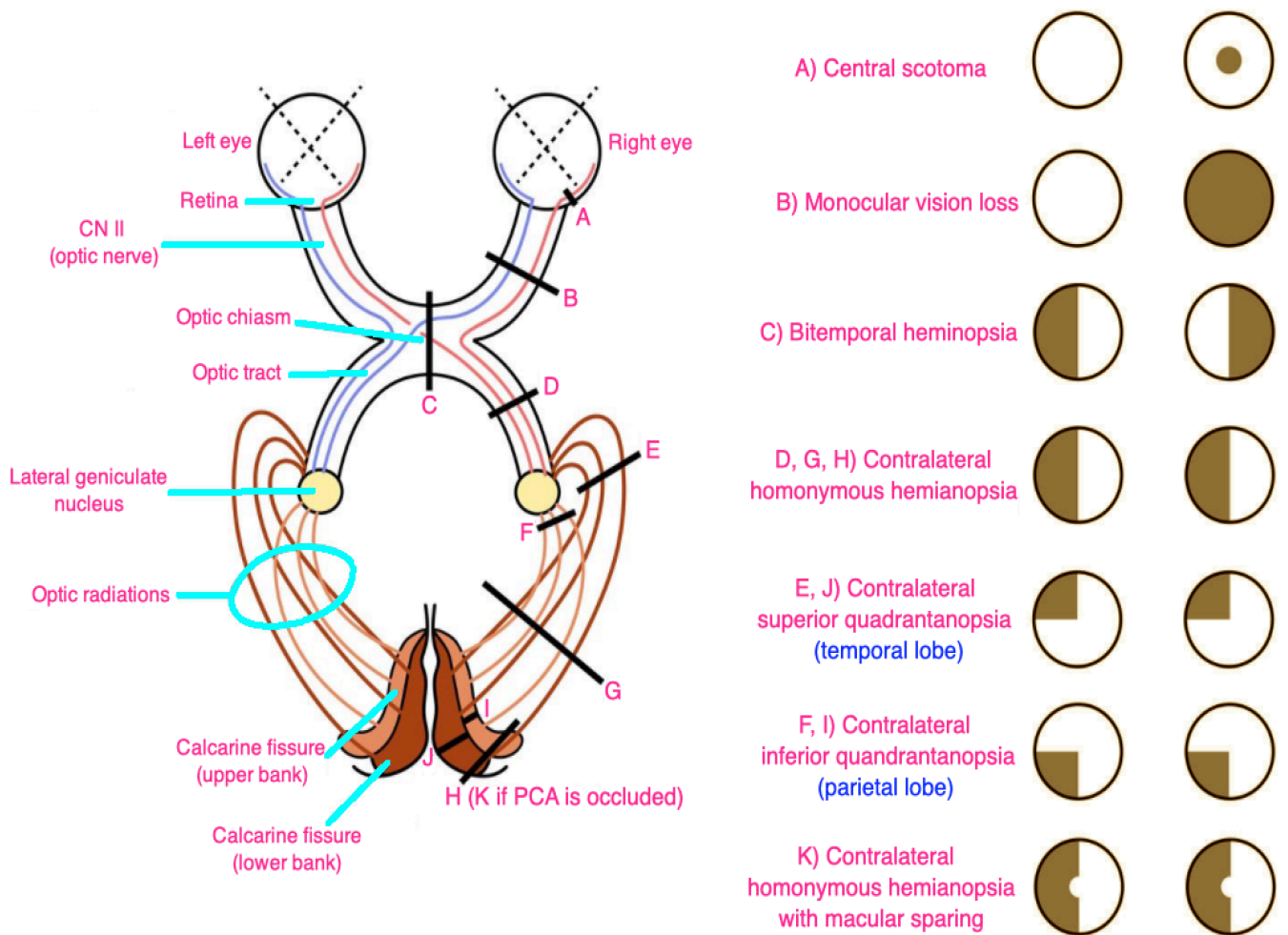
Opioid receptor agonists

Morphine	<ul style="list-style-type: none"> - Gold standard opioid; used for moderate to severe pain. - USMLE wants you to know that morphine is "metabolized into active metabolites that accumulate." This is NBME answer for how overdose can occur in patients who use self-controlled pumps, since it can take time to work, so patient uses too much. - Patients who are in severe pain can sometimes have hypertension as a result. Surgery Q has morphine as answer for how to control BP post-op. - If patient has history of opioid abuse but has severe pain, e.g., due to trauma, do not withhold using opioids. Always treat pain fully.
Codeine	<ul style="list-style-type: none"> - Less potent than morphine; used for mild to moderate pain; in many antitussives.
Oxycodone	<ul style="list-style-type: none"> - Potent opioid often combined with acetaminophen. - USMLE wants you to know that oxycodone/acetaminophen combo is preferred initially in patients who are post-op. Do not just jump to morphine.
Fentanyl	<ul style="list-style-type: none"> - Potent synthetic opioid with high abuse potential.
Meperidine	<ul style="list-style-type: none"> - Potent opioid with high abuse potential. - I've noticed NBME likes this opioid for malingering Qs, where they'll say, e.g., a 47-year-old man comes into the ER in severe pain requesting meperidine.

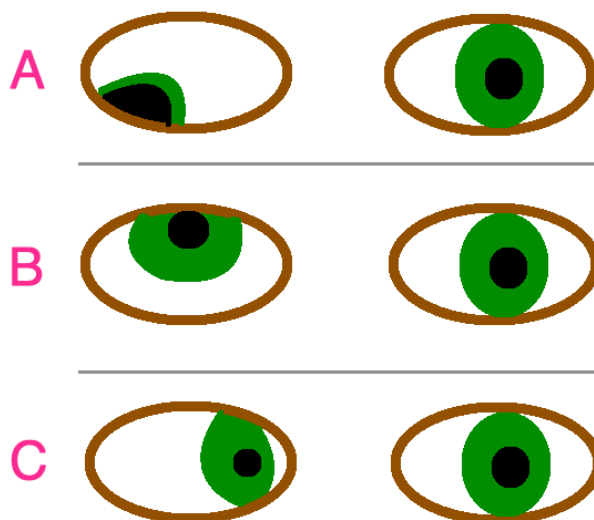
Dextromethorphan	<ul style="list-style-type: none"> - Opioid used in antitussives. - Common cause of delirium from over-the-counter cold meds.
Loperamide, eluxadoline	<ul style="list-style-type: none"> - Opioids used for diarrhea-predominant irritable bowel syndrome. - Low addictive potential. - The fact that opioids cause constipation as an adverse effect "is a good thing" in the setting of wanting to help limit diarrhea in IBS.
Buprenorphine	<ul style="list-style-type: none"> - Mu partial agonist and kappa antagonist. - The kappa antagonism can help cause less dysphoria. - NBME Q floating around somewhere wants you to know it has the kappa effects.
Tramadol	<ul style="list-style-type: none"> - Unique MOA where it is weak mu opioid agonist + also an SNRI.
Methadone	<ul style="list-style-type: none"> - Long-acting full mu opioid agonist that is used for opioid/heroin withdrawal. - Reduces opioid cravings.
Opioid receptor antagonists	
Naloxone	<ul style="list-style-type: none"> - Opioid receptor antagonist used for acute overdoses.
Naltrexone	<ul style="list-style-type: none"> - Opioid receptor antagonist used for alcohol dependence (i.e., ↓ alcohol cravings). - Can also be used for opioid dependence in patients who are already detoxified in order to prevent relapse (i.e., by blocking opioid receptors, if the patient abuses any opioids, he/she won't feel the euphoric effects).
Suboxone	<ul style="list-style-type: none"> - Buprenorphine + naloxone combo given orally for opioid addiction in those who have high risk of abuse, or those who have already abused methadone. - Buprenorphine's partial agonist effects at mu receptors help with cravings, but the naloxone is added so that if the patient crushes the suboxone and injects it, the naloxone will antagonize the opioid receptors and cause withdrawal symptoms. However, when taken orally, the naloxone has negligible effect due to poor oral bioavailability.

Alcohol abuse drugs	
Disulfiram	<ul style="list-style-type: none"> - Blocks acetaldehyde dehydrogenase. - If patient drinks while on the drug, he/she will experience flushing + severe discomfort, thereby disincentivizing any form of drinking.
Acamprosate	<ul style="list-style-type: none"> - Alcohol inhibits NMDA glutamate receptor activity, where chronic alcoholism causes upregulation of NMDA receptors and excessive glutamate transmission and excitotoxicity upon withdrawal. - Acamprosate decreases alcohol withdrawal cravings by modulating glutamatergic activity.
Naltrexone	<ul style="list-style-type: none"> - As mentioned above, opioid receptor antagonist that ↓ alcohol cravings.

IM Ophthal

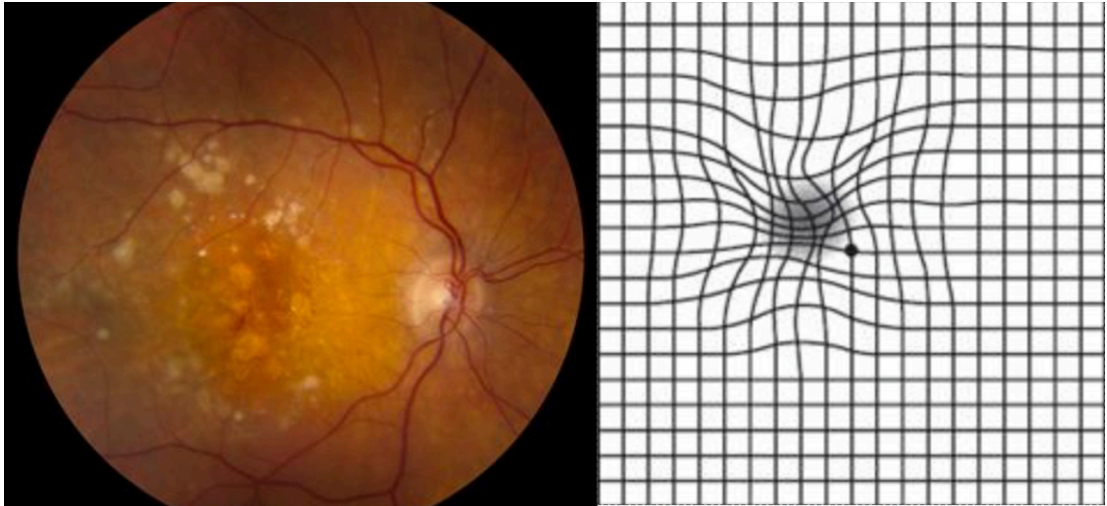


Extraocular nerve palsies



- A = CN III (oculomotor) lesion → presents as down and out.
- B = CN IV (trochlear) lesion → presents as upward gaze + patient will tilt head toward unaffected side.
- C = CN VI (abducens) lesion → medially directed eye.

Glaucoma	
Open-angle	<ul style="list-style-type: none"> - Chronic eye condition characterized by increased intraocular pressure due to impaired drainage of aqueous humor. - Unlike acute angle-closure (closed-angle) glaucoma, the drainage angle (canal of Schlemm) between the cornea and iris remains open. - Progresses slowly and is usually painless. - As it advances, causes peripheral vision loss (tunnel vision) and results in optic nerve damage characterized by “cupping of the optic disc” (i.e., an increased cup-to-disc ratio). - The USMLE wants tonometry as the first step in management (measures intraocular pressure). - Treatment for open-angle glaucoma for USMLE is not going to be a trivia game of “which drug first.” They just want you to know that topical prostaglandins, such as latanoprost, can increase outflow of aqueous humor, thereby reducing IOP. - Topical beta-blockers, such as timolol, decrease production of aqueous humor. - Carbonic anhydrase inhibitors, such as dorzolamide, decrease production of aqueous humor. - Pilocarpine is a muscarinic receptor agonist that constricts the pupil and increases outflow of aqueous humor.
Closed-angle	<ul style="list-style-type: none"> - Presents on USMLE as a very buzzy red, teary, fixed mid-dilated pupil. - Due to closure of the drainage angle (canal of Schlemm) between the cornea and the iris, leading to a rapid increase in IOP. - Can lead to compression of the optic nerve and blood vessels, causing severe symptoms such as intense eye pain, headache, nausea, vomiting, blurred vision, and seeing colored rings or halos. - Similar to open-angle glaucoma, the USMLE wants tonometry as the first step to confirm increased IOP. - Treatment is IV mannitol (helps draw excess aqueous humor out of the eye), timolol, pilocarpine (muscarinic receptor agonist), or alpha-2 agonists such as brimonidine.

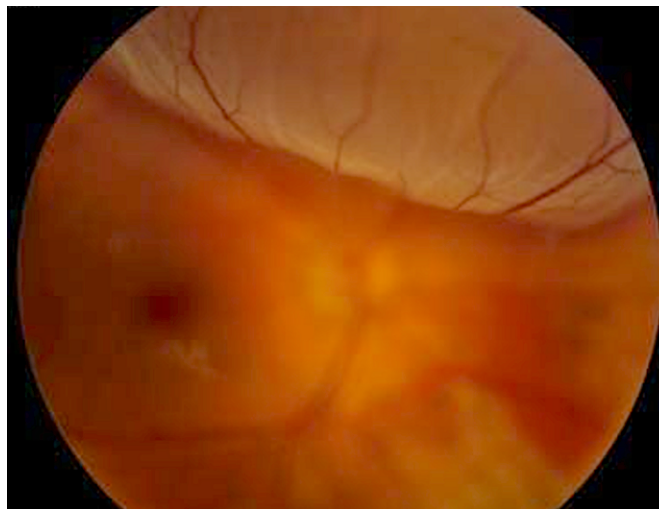
Macular degeneration	
<p>- USMLE wants you to know that “wavy lines” on a straight-line Amsler test = macular degeneration.</p>	
	
<ul style="list-style-type: none"> - It is characterized by loss of central vision. - Fundoscopy shows drusen, which are yellow lipoproteinaceous deposits. - There are dry (atrophic) and wet (neovascular) types of macular degeneration. - Most commonly occurs idiopathically due to age (i.e., age-related macular degeneration). - Dry is treated supportively; wet is treated with anti-VEGF agents and sometimes laser therapy. 	

Retinitis pigmentosa

- Presents on USMLE as a combo of nyctalopia (loss of night vision) and loss of peripheral vision.
- There will often be a family history. Fundoscopy shows characteristic pigmentation.

**Retinal detachment**

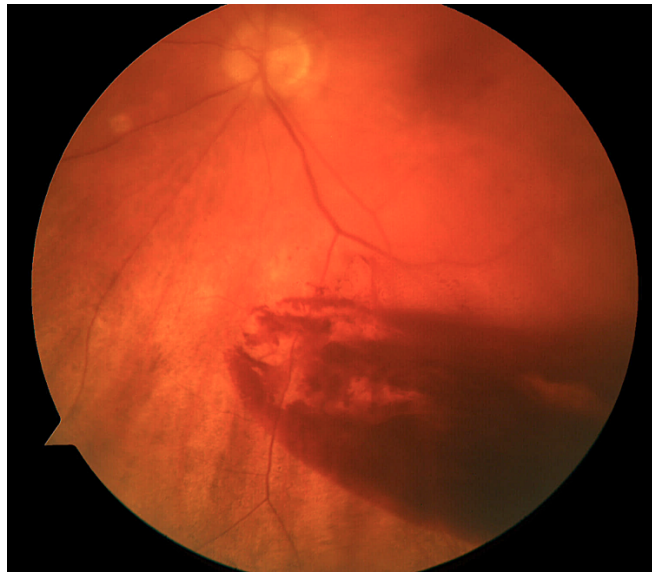
- Occurs classically in those with sudden trauma to the eye or severe myopia.
- The fundoscopy is HY and important for USMLE, especially 2CK.



- Treatment is surgical and includes pneumatic retinopexy (i.e., gas bubble is injected into the eye to push the retina back into place; scleral buckling (piece of silicone is attached to the sclera to exert posteriorly-directed pressure so the retina reattaches); and vitrectomy (vitreous humor is removed and replaced with gas or silicone oil to flatten the retina).

Vitreous hemorrhage

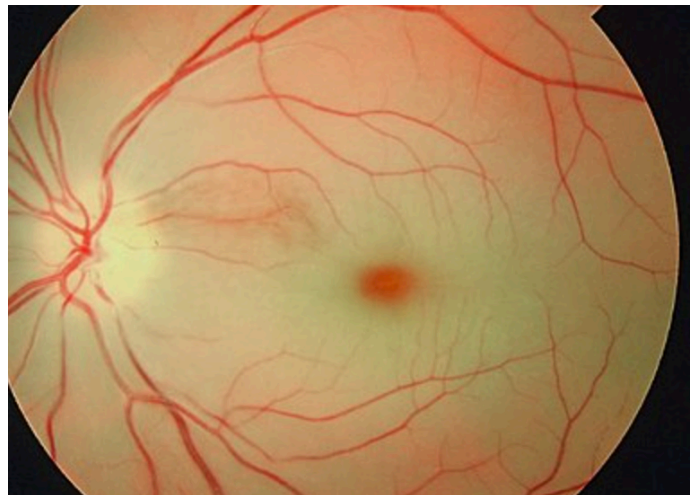
- USMLE wants you to know that the biggest risk factors for bleeding into the vitreous are diabetes and hypertension.



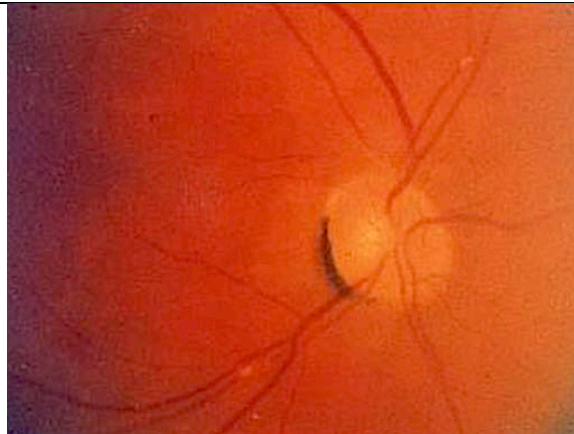
- Vitreous hemorrhage will usually be a distractor, where they can tell you a young boxer was hit in the eye, but the answer is retinal detachment, not vitreous hemorrhage.

Central retinal artery occlusion

- Presents as sudden, painless vision loss in a patient where a "curtain comes down."
- Due to a carotid atheroma (in setting of HTN) or left atrial mural thrombus (in setting of atrial fibrillation) that's launched off to the retinal vessels.
- A pale retina will be seen on fundoscopy with a cherry red spot due to maintenance of perfusion from the choroidal artery.



- Ocular massage can be attempted as Tx, where the embolus may be dislodged, restoring perfusion.



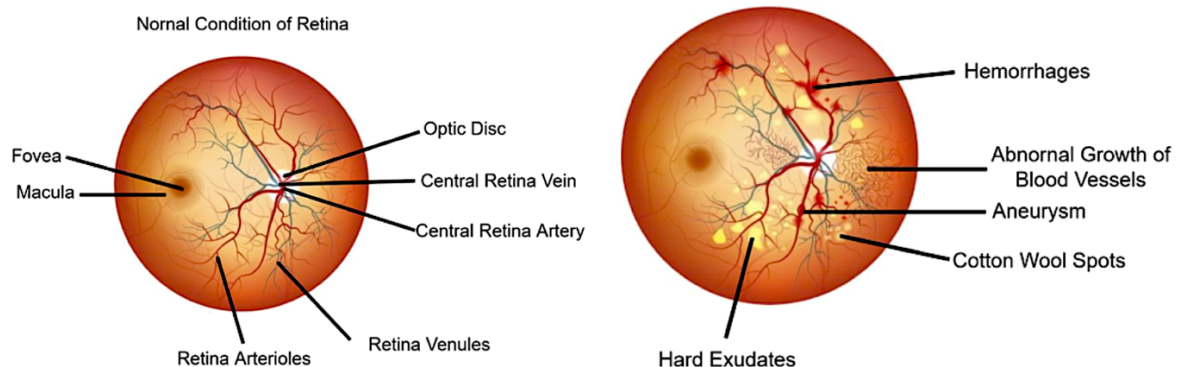
- USMLE can show image that looks similar to this one. They want you to know that weird crescent-shaped finding is called a "refractile body," and refers to an embolus.

Diabetic retinopathy

- Can present in numerous ways, such as with blurred or fluctuating vision, and difficulty recognizing colors.
- The USMLE vignette will usually say things like cotton wool spots (soft exudates), hard exudates, and retinal hemorrhages.
- Soft exudates are small, whitish lesions on the retina caused by microinfarctions and are axoplasmic material; hard exudates are lipoproteinaceous deposits due to leaky retinal vessels.
- Soft/hard exudates and retinal hemorrhages are seen classically in both diabetic and hypertensive retinopathies.



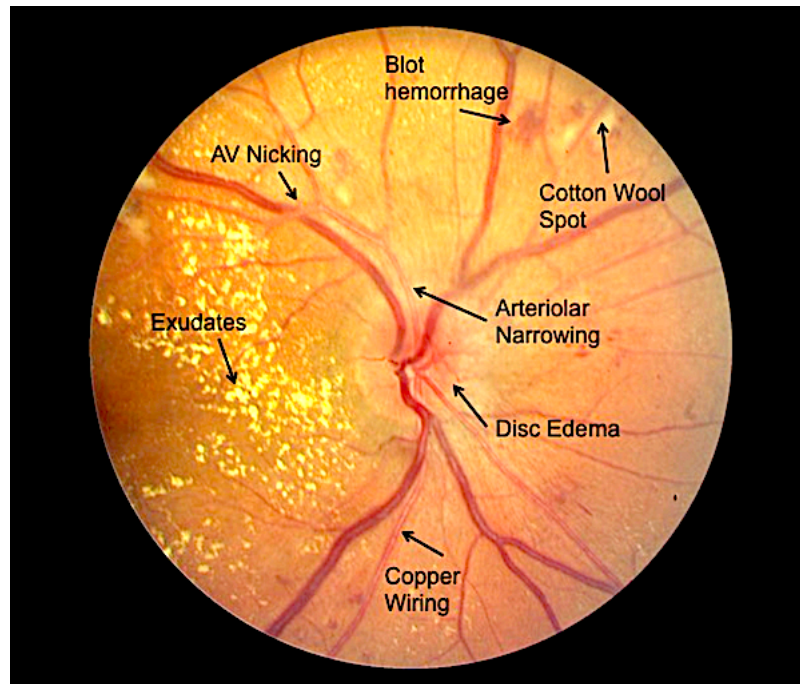
Diabetic Retinopathy



- Can be dry or wet (neovascular). Wet type can be treated with anti-VEGF agents.

Hypertensive retinopathy

- Buzzy findings like AV nicking and arteriolar narrowing.
- Q can mention “sausage-like” appearance of retinal arterioles.



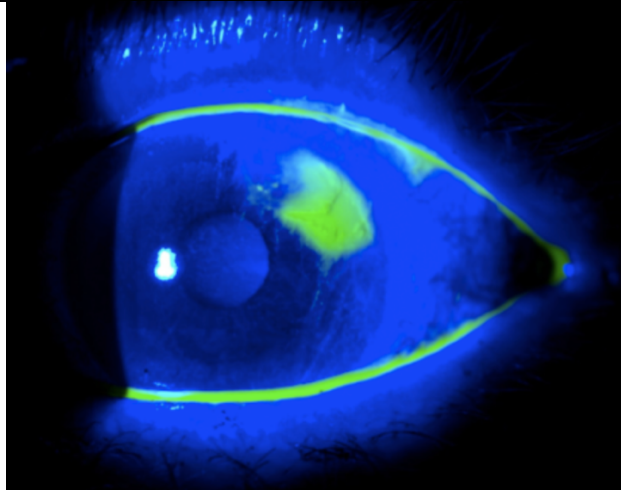
Dyslipidemia

- Orbital xanthoma (cholesterol deposits; left image) and corneal arcus (lipid deposits; right image).
- Both can occasionally be seen idiopathically in patients without lipid disorders (the latter in elderly).



Corneal abrasion

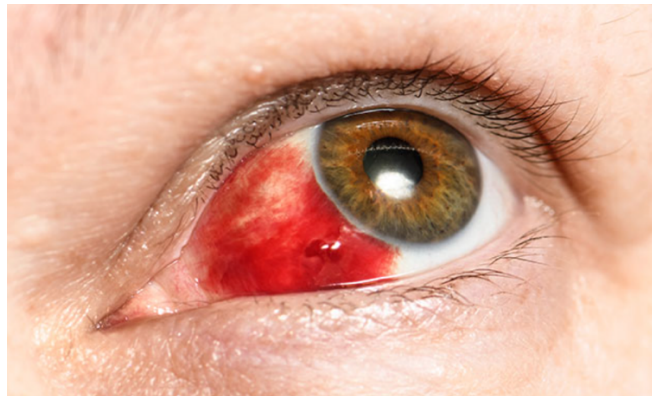
- Scratchy or tearing sensation of the eye. Can be caused by contact lens-use or coming into contact with irritants such as sand (i.e., playing in sandbox with son/daughter).
- USMLE will either ask for the next best step, where the answer is “instillation of fluorescein into the eye,” or they will show you the following image (which is a fluorescein instillation) and then just ask for the diagnosis (i.e., corneal abrasion).



- Fluorescein is an orange dye that when dripped into the eye appears blue-green under violet light.
- Anything blue is normal. Anything green is abnormal.

Subconjunctival hemorrhage

- Buzzy image / spot-diagnosis for USMLE.
- Caused by bursting of superficial conjunctival vessels. Looks sinister but self-resolves uneventfully.
- Can be caused by trauma or brief periods of increased pressure (i.e., severe vomiting or coughing).

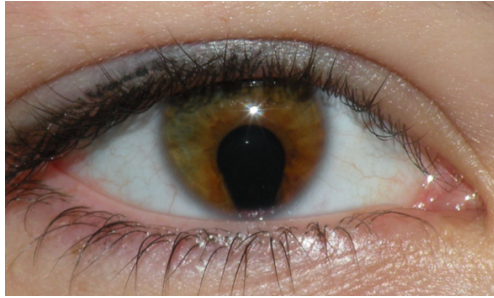

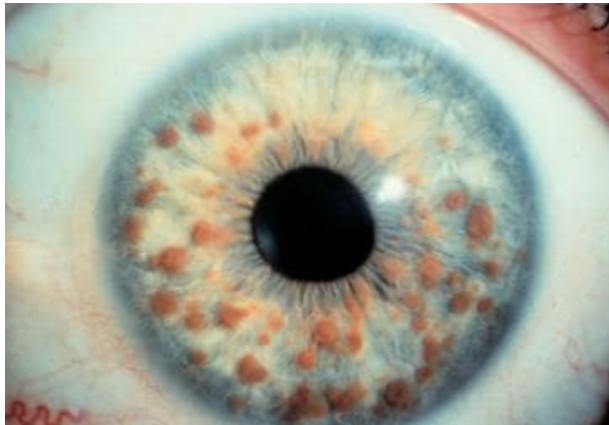


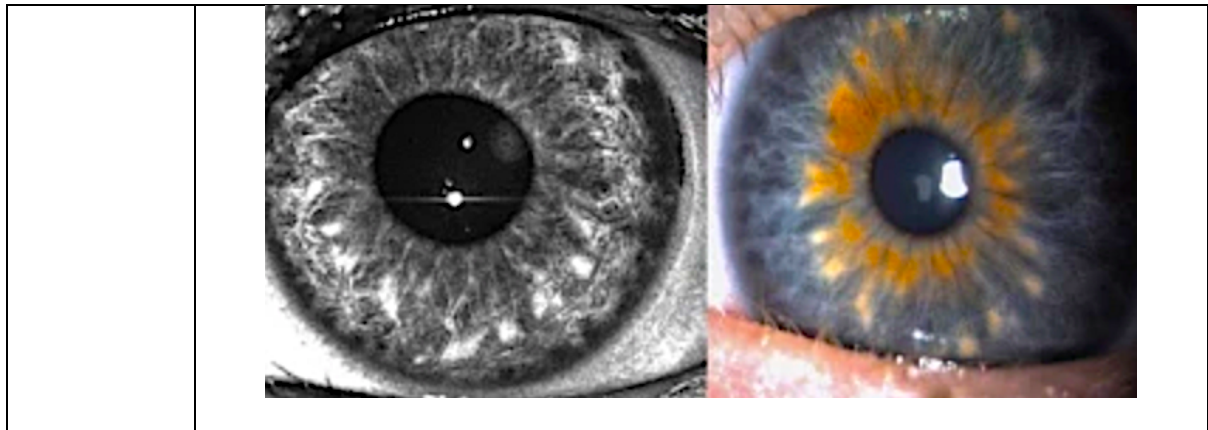
Iris abnormalities



Aniridia



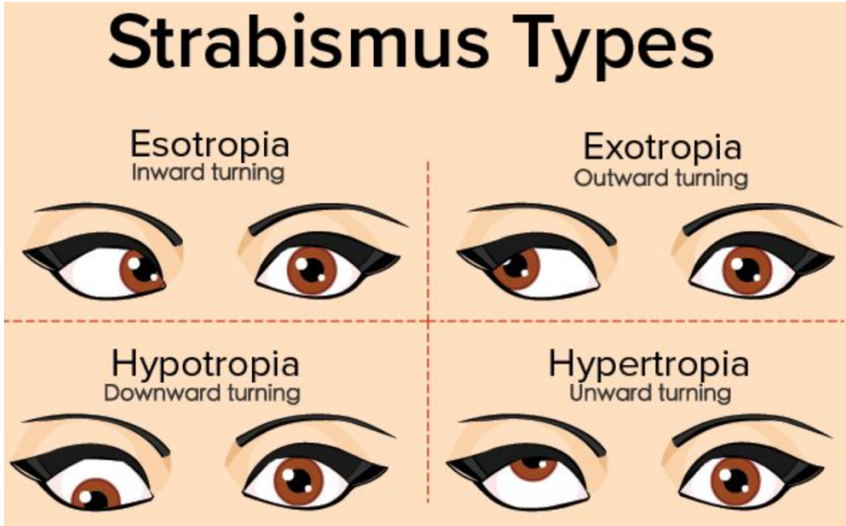
- Seen as part of **WAGR** complex with *WT1* mutations – i.e., **W**ilms tumor, **A**niridia, **G**enitourinary anomalies, **R**etardation.




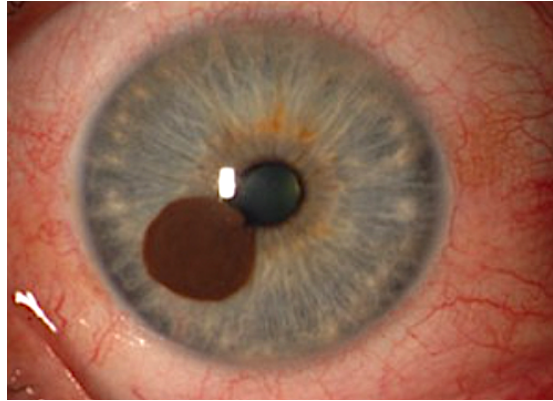
Coloboma	<p>- Means hole in the eye. Seen in CHARGE syndrome, → Coloboma of the eye, Heat defects, Atresia of the choanae, Retardation of growth and development, Genitourinary anomalies, Ear defects.</p> 
Albinism	<p>- Can cause pale blue or pink irides (pleural for iris).</p> 
Lisch nodules	<p>- Iris hamartomas seen in NF1.</p>  <p>- NF1 can present with axillary and groin freckling, café au lait spots (hyperpigmented macules), optic glioma (tumor of CN II), neurofibromas (nodules under the skin), pheochromocytoma, and weird brain cancers such as ependymoma and oligodendroglioma.</p>
Brushfield spots	<p>- Connective tissue deposits seen within the irides of some patients with Down syndrome.</p>

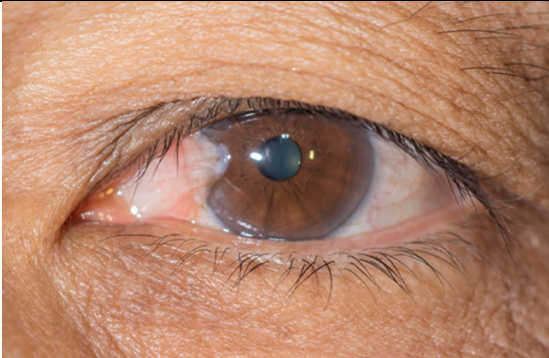



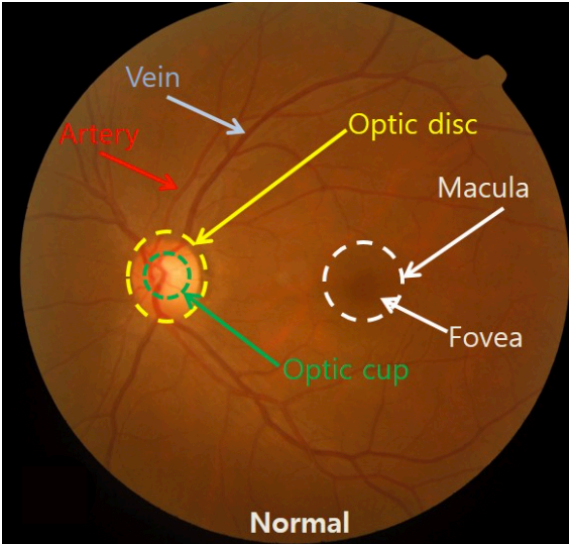
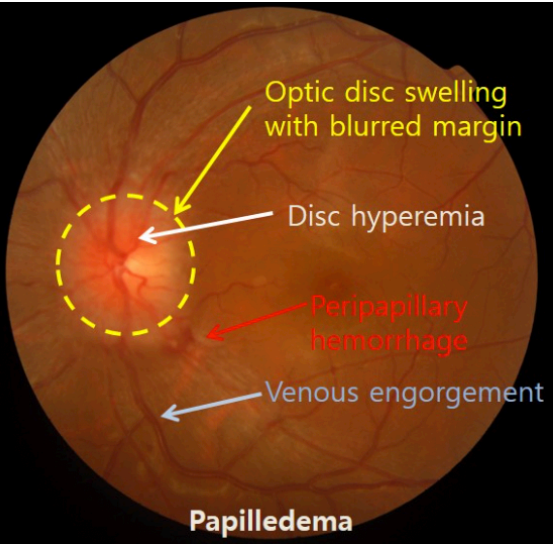
HY Peds Ophthal Ddx for IM	
Orbital cellulitis	 <ul style="list-style-type: none"> - Infection involving tissues posterior to orbital septum; <i>Staph aureus</i> most common cause; rare sequela of adjacent infection, e.g., from the paranasal sinus; medical emergency; requires IV antibiotics; preseptal cellulitis is a less severe version of orbital cellulitis.
Hordeolum (stye)	<ul style="list-style-type: none"> - Painful bump on the eyelid. - <i>Staph aureus</i> infection of sweat gland or oil duct; treat with warm compresses. - Can occur any age. 


Chalazion	 <ul style="list-style-type: none"> - Painless bump on the eyelid. - Blocked oil duct; not an infection; treat with warm compresses.
Retinoblastoma	 <ul style="list-style-type: none"> - The image shows leukocoria, which is an abnormal white appearance of the eye on light reflex (should normally appear red). - USMLE wants you to know that <i>RB</i> gene mutations not only cause congenital retinoblastoma, but also ↑ risk of osteosarcoma. - In other words, classic Q is they show you image above + ask what child is at risk for later → answer = osteosarcoma.
Strabismus	<p>- Means "lazy eye," or misalignment of the eyes, due to weakened muscles in one eye.</p> 

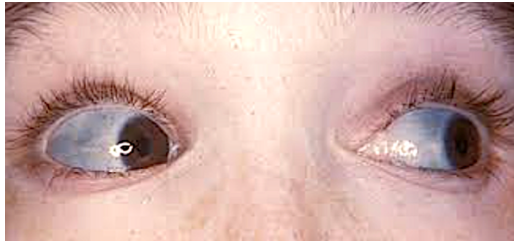
	<ul style="list-style-type: none"> - Can lead to amblyopia, which is reduced visual acuity in the weak eye due to the brain favoring the stronger eye during development. - Strabismus, however, is not reduced vision in the weak eye. It precedes amblyopia if not treated with eye exercises and/or penalization of (patching) the strong eye.
--	---

UV light-induced Ophthal pathologies	
Cataracts	<ul style="list-style-type: none"> - Progressive clouding or opacification of the lens, leading to blurred or hazy vision, particularly in bright light, with increased glare sensitivity.  <ul style="list-style-type: none"> - Can be caused by sunlight, but the most important cause on USMLE is diabetes mellitus, since high glucose entering the lens → converted to sorbitol via aldose reductase → sorbitol has high osmotic pull, causing osmotic damage to the lens and cataracts. - Recent changes in visual acuity can suggest new-onset or worsening diabetes. - Can be seen in Peds in congenital rubella, congenital syphilis, and NF2.
Melanoma	<ul style="list-style-type: none"> - Melanomas can grow from the conjunctiva and cornea. Just be aware they exist. 
Pterygium	<ul style="list-style-type: none"> - Non-cancerous overgrowth of non-keratinized stratified squamous epithelium growing from the conjunctiva. - Crosses over the cornea (clear part of the eye covering the iris and pupil). - History of sun exposure is the major risk factor.

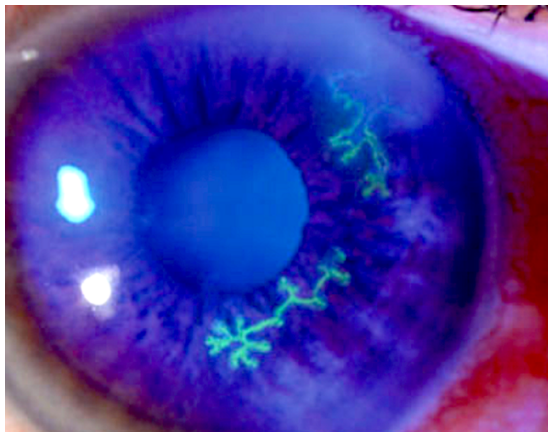
	
Pinguecula	<div><ul style="list-style-type: none">- Yellow-white benign lesion on the conjunctiva composed of protein and fat.- Does not cross over the cornea.- Sunlight is the major risk factor.</div> 

Papilledema	
<ul style="list-style-type: none">- Means increased intracranial pressure on USMLE.- Papilledema refers to blurring of the optic disc margins due inflammation of the optic nerve head in the setting of increased intracranial pressure.	
	

HY Autoimmune eye pathologies	
Anterior uveitis	<ul style="list-style-type: none"> - WBCs in the anterior chamber sometimes seen in flares of autoimmune diseases, especially sarcoidosis and ankylosing spondylitis. - USMLE might sometimes just give you patient with sarcoidosis and then ask what needs to be done in terms of follow-up for the patient → answer = “slit-lamp examination” to check for anterior uveitis.
Keratoconjunctivitis sicca	<ul style="list-style-type: none"> - Dry eye (xerophthalmia) caused by decreased tear production. - Classically autoimmune, either a stand-alone condition or as part of Sjögren syndrome. - Latter presents additionally with dry mouth (xerostomia) and systemic findings such as arthritis.
Dermatomyositis	<ul style="list-style-type: none"> - Causes heliotrope rash (violaceous eyelids). - Don't confuse with the malar rash of lupus.  <ul style="list-style-type: none"> - Violaceous eyelids can also be seen in neuroblastoma in Peds, albeit completely unrelated. I just mention it cuz it shows up on an NBME form.

Miscellaneous hereditary conditions	
Leber hereditary optic neuropathy	<ul style="list-style-type: none"> - USMLE wants you to know that mitochondrial disorders, e.g., LHON, present as a triad of 1) eye/ear problems, 2) hypotonia, and 3) lactic acidosis (low bicarb; metabolic acidosis). - Other mitochondrial disorder names you could be aware of are MELAS (Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like episodes) and MERRF (Myoclonic epilepsy with ragged red fibers). - Heteroplasmy is variability of phenotype severity across offspring.
Osteogenesis imperfecta	<ul style="list-style-type: none"> - Collagen I mutation. - Can cause the very buzzy blue sclerae. 
Alport syndrome	<ul style="list-style-type: none"> - Mutation in type IV collagen; X-linked recessive. - The answer on USMLE for eye and/or ear problem + red urine.
Marfan syndrome	<ul style="list-style-type: none"> - Can cause lens dislocations.
Homocystinuria	<ul style="list-style-type: none"> - Can cause lens dislocations.

Ophthalmia neonatorum	
- Fancy way of saying neonatal conjunctivitis.	
Chlamydia	<ul style="list-style-type: none"> - Caused by <i>C. trachomatis</i> D-K (the STD). - Presents usually >1 week post-birth and can lead to pneumonia with a lymphocytic shift (since chlamydia is obligate intracellular, so requires lymphocytes for cell-mediated immunity to clear them, unlike extracellular bacteria which can be cleared humorally with neutrophils). - The chlamydia can drain through the nasolacrimal duct down to the lungs, causing the pneumonia. - Prophylaxis is treating the mom while pregnant if she has chlamydia; treatment in the neonate who already has the conjunctivitis is oral erythromycin. - NBME can give you vignette of wheezes, crackles, and fever in a 3-week-old who they say was treated for chlamydia conjunctivitis 2 weeks ago with topical erythromycin at birth. But this is not the correct treatment since topical will not cover any organism that has already entered the nasolacrimal duct.
Gonorrhea	<ul style="list-style-type: none"> - Gonococcal conjunctivitis will present in the first week of life with yellow discharge from the eye(s). - The USMLE vignette will be vague, where the student says, "But how are we supposed to know it's not chlamydia, just because it's first week of life, that's it?" And my response is: if they give you chlamydia ophthalmia neonatorum, they'll always tie it to subsequent pneumonia somehow, since that is such a HY point. - Prophylaxis for gonococcal is erythromycin ointment; treatment is IM 3rd-gen cephalosporin (usually cefotaxime in peds).
Chemical	- Chemical conjunctivitis is classically due to silver nitrate eyedrops that used to be given to neonates for gonococcal prophylaxis. However, they have been replaced by erythromycin ointment.
Viral	- Viral conjunctivitis will present as teary eye that is either unilateral or bilateral, and either itchy or non-itchy. I've seen variable presentation on USMLE. You just need to know this is the most likely diagnosis in both school-age kids and adults, and is caused by adenovirus , which is a DNA virus. Treatment is supportive with saline rinse.
Allergic	<ul style="list-style-type: none"> - USMLE wants you to know that "cobblestoning" of the tarsal conjunctiva is buzzy for allergic conjunctivitis. - Likewise, for allergic rhinitis, they can say cobblestoning of the nasal mucosa. - Some students have asked if allergic has to be bilateral, which it need not. And it doesn't have to be itchy either.

Herpesviridae infections	
Herpes keratitis	<ul style="list-style-type: none"> - Keratitis is inflammation of the cornea. - HSV1/2 can cause dendritic (tree-like) pattern in the eye on fluorescein instillation. 

	<ul style="list-style-type: none">- May or may not cause vesicles around the eye as well.- Tx with topical acyclovir/valacyclovir.
Herpes zoster ophthalmicus	<ul style="list-style-type: none">- VZV (HHV-3) can cause shingles of the eye.- Causes keratitis with a similar dendritic pattern to HSV 1/2.- May or may not cause vesicles around the eye as well.- Tx with topical acyclovir/valacyclovir.
CMV retinitis	<ul style="list-style-type: none">- The answer for blurry vision in severely immunocompromised patient (usually AIDS).- You don't need to know the fundoscopy.- Treat with ganciclovir.

IM MSK

Rotator cuff injuries		
Rotator cuff muscles (SITS)	Function	HY Points
Supraspinatus	Abduction of arm (first 15 degrees)	<ul style="list-style-type: none"> - Answer if patient has difficulty abducting arm first 15 degrees. - Empty-can (thumb-down) / full-can (thumb-up) tests for diagnosis → patient abducts arm to 90 degrees with thumb up or down → downward pressure applied to arm → if elicits pain, answer = supraspinatus injury. - There is Q on new 2CK CMS IM form 7 where answer is supraspinatus tendonitis, and they say patient has reduced ability to abduct the first 60 degrees.
Infraspinatus	Lateral (external) rotation	<ul style="list-style-type: none"> - Notion of “pitcher injury” = infraspinatus does more harm than good for USMLE; vignette can by all means give a pitcher with (+) full-can test above and answer is supra-, not infra-, spinatus injury. - Q might say patient simply cannot externally rotate arm, nothing more, where teres minor isn’t listed as another answer, so infraspinatus is only one that could be right.
Teres minor	Adduction; lateral rotation	<ul style="list-style-type: none"> - Same as infraspinatus, just know it externally rotates the arm. - Also adducts arm, so if patient has issues with both lateral rotation and adduction, answer is teres minor over infraspinatus. - I’ve never seen NBME material assess the diagnostic tests for infraspinatus or teres minor.
Subscapularis	Adduction; medial (internal) rotation	<ul style="list-style-type: none"> - Can medially rotate and adduct the arm. - I’ve had students get asked Gerber lift-off test on both Steps, where the answer = subscapularis. - Gerber lift-off test = patient places dorsal aspect of hand on lower back, with palm facing posteriorly → examiner applies pressure into the patient’s palm against his/her lower back → patient is then asked to move hand away under the pressure → if elicits pain / difficult to do, answer = subscapularis injury.

Upper limb nerve HY Points for Surg	
Axillary	<ul style="list-style-type: none"> - Main innervation of the deltoid, allowing for abduction of arm 15-90 degrees. USMLE wants you to know deltoid has an origin on the lateral clavicle and axillary nerve innervating it is at C5/C6. - Palsy caused by surgical neck of humerus fracture. - USMLE vignette will often say “flattened deltoid” or “loss of sensation over lateral upper arm / deltoid.”
Median	<ul style="list-style-type: none"> - Main innervation is lateral “3 and a half” fingers / thenar pad, and lateral forearm. - Does thumb abduction. (In contrast, ulnar nerve does thumb adduction) - NBME wants “palmar cutaneous branch of median nerve” as answer for sensation over thenar region. - Palsy caused by supracondylar fracture of humerus, or “distal shaft fracture.” Former is buzzy; latter sounds non-specific, but I’ve seen it this way on NBME. - Entrapment of median nerve causes carpal tunnel syndrome; will present as paresthesia/numbness of lateral hand / thenar region; can be caused by hypothyroidism (GAG deposition), acromegaly (growth of tendons), and pregnancy (edema); can occur bilaterally in construction workers using jackhammer. - Tx for carpal tunnel ultra-HY on 2CK. “Use of wrist pad when using computer” is answer on new 2CK NBME. If not listed, “wrist splint” is answer. If vignette says wrist splint fails, NSAIDs are wrong answer and not proven. USMLE wants “triamcinolone

	<p>injection into carpal tunnel” (not IV steroids) as next answer. Surgery is always wrong answer for carpal tunnel on USMLE.</p> <p>- 2CK wants “electrophysiological testing” and “electromyography and nerve conduction studies” as next best step in diagnosis for carpal tunnel.</p>
Ulnar	<p>- Main innervation of medial “1 and a half” fingers, and medial forearm.</p> <p>- Ulnar nerve also does finger abduction and adduction (i.e., interosseous muscles).</p> <p>- USMLE loves Froment sign for ulnar nerve injury, which is inability to pinch a piece of paper between the thumb and index finger (ulnar nerve needed for thumb adduction against index finger, despite thumb being most lateral digit).</p> <p>- Distal compression (i.e., of wrist and hand only, not forearm) is aka Guyon canal syndrome and is caused by hook of hamate fracture; this can sometimes be seen in cyclists due to handlebar compression; presents as paresthesias / numbness of 4th and 5th fingers + hypothenar eminence.</p> <p>- Proximal compression (i.e., medial forearm + wrist/hand) is aka cubital tunnel syndrome and is one of the most underrated diagnoses on USMLE, since its yieldness, especially on 2CK, is comparable to carpal tunnel syndrome, but students often haven’t heard of it. Essentially, patient will get paresthesias of medial forearm + hand, where it “sounds like carpal tunnel but on the ulnar side instead” → answer = cubital tunnel syndrome.</p> <p>- Tx for cubital tunnel syndrome is “overnight elbow splint.” Surgery is wrong answer on USMLE.</p>
Radial	<p>- Main innervation for finger, wrist, and elbow extension.</p> <p>- Innervates BEST → Brachioradialis, Extensors, Supinator, Triceps.</p> <p>- Palsy occurs as a result of midshaft fracture of the humerus, or as a result of fracture at the radial groove (latter is obvious).</p> <p>- Retired NBME Q says construction worker sustains “comminuted spiral fracture of humerus” (unusual, since spiral fracture classically = child abuse), and they ask for the resulting defect → answer = “loss of radial nerve function.”</p> <p>- Highest yield point is that injury results in pronated forearm + wrist drop.</p>
Musculocutaneous	<p>- Main innervation of the biceps.</p> <p>- Just need to know injury results in loss of sensation over lateral forearm + decreased biceps function.</p> <p>- USMLE doesn’t give a fuck about what kind of injury causes palsy.</p>

Frequently confused shoulder conditions	
Subacromial bursitis vs rotator cuff tendonitis	<p>- In NBME vignettes, I’ve seen both can give Hx of patient doing frequent overhead movement (i.e., painting a fence) + pain with palpation + pain that’s worse when lying on one’s shoulder in bed at night, making differentiating these difficult.</p> <p>- Subacromial bursitis will only present with above findings, which collectively are known as impingement syndrome.</p> <p>- Rotator cuff tendonitis will present with weakness when performing exam maneuvers (as described in prior table).</p>
Biceps tendonitis	<p>- Presents as anterior shoulder pain with focal tenderness over the biceps tendon (i.e., when pressing on anterior shoulder).</p>
Adhesive capsulitis	<p>- Aka “frozen shoulder,” or arthrofibrosis.</p> <p>- Decreased passive and active motion of shoulder in all directions.</p> <p>- Idiopathic, but increased risk in diabetes.</p> <p>- Tx = range of motion exercises / physiotherapy.</p>

Winged scapula**Winged scapula**

- Long thoracic nerve injury, which innervates serratus anterior.
- Can occur post-mastectomy.

Brachial plexus injuries

- Both can be caused in neonates by breech / traumatic labor.
- Can also be caused by injuries such as grabbing onto tree branch while falling.

Erb-Duchenne

- Upper brachial plexus injury (C5-C6).
- Sometimes rather than Erb-Duchenne written as the diagnosis, the answer will just be "upper brachial plexus" when they ask for what's injured.



**"Waiter's tip"
deformity**

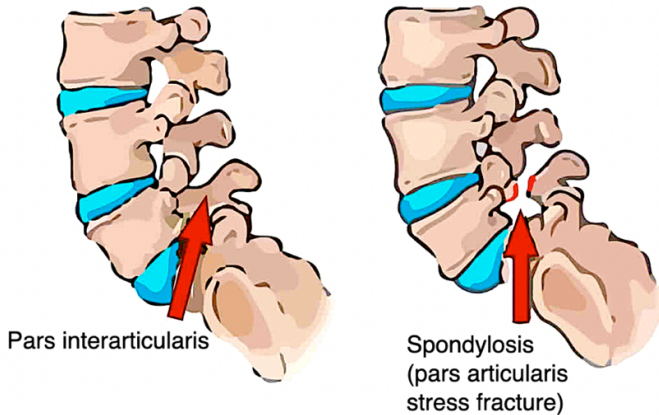
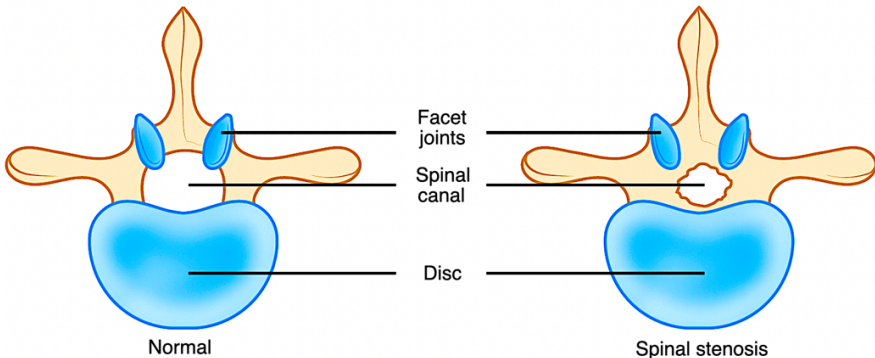
- Arm is adducted, pronated, and wrist flexed.

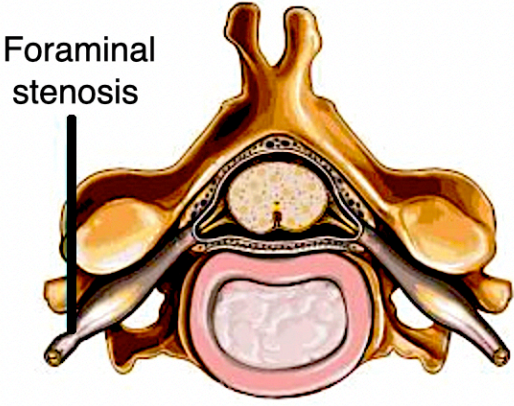
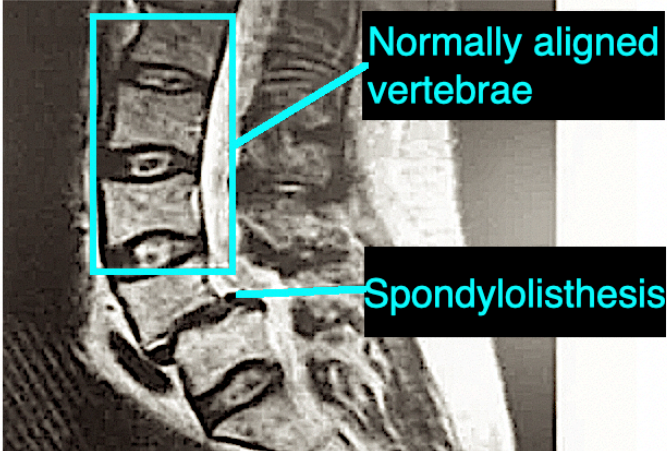
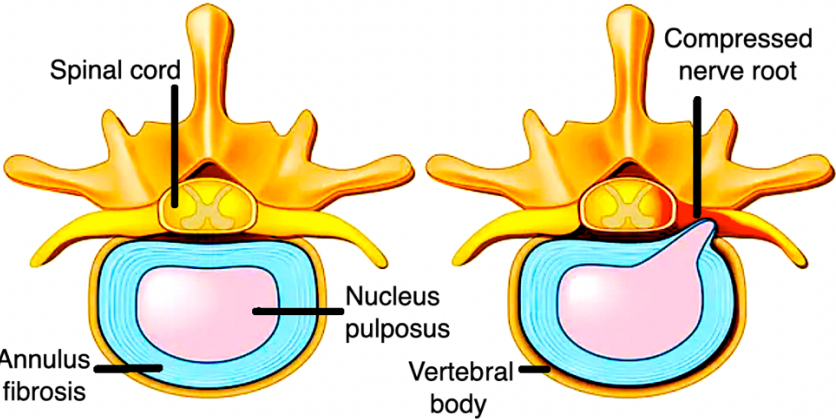
Klumpke

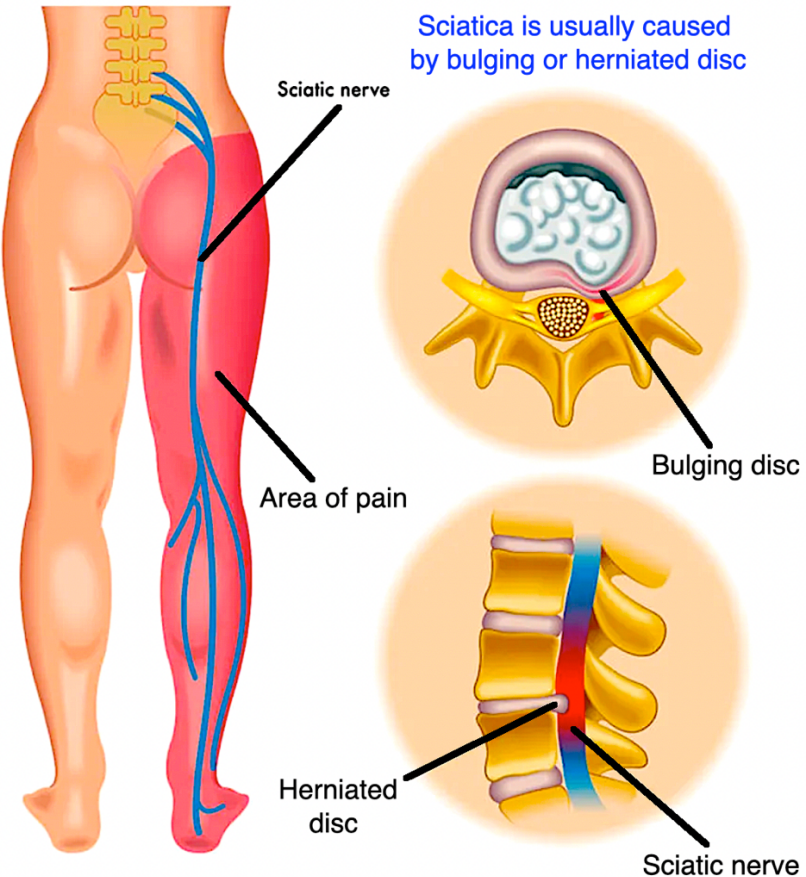
- Lower brachial plexus injury (C8-T1).
- Sometimes rather than Klumpke written as the diagnosis, the answer will just be "lower brachial plexus" when they ask for what's injured.

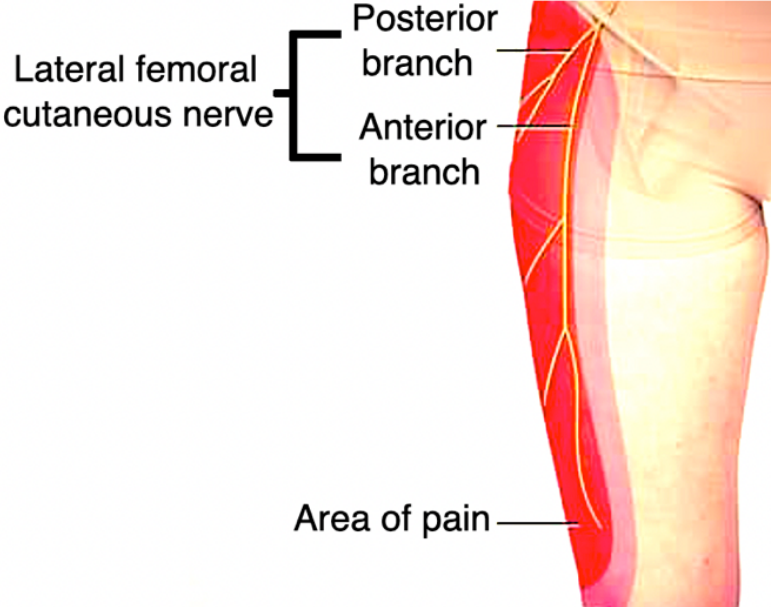
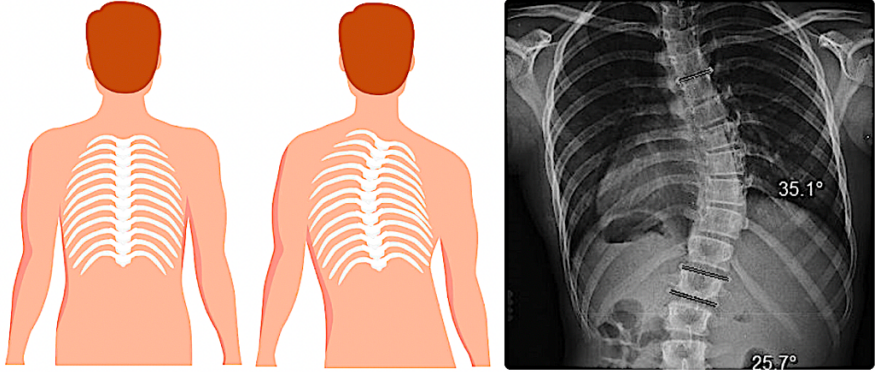
**Klumpke
"claw-hand"**

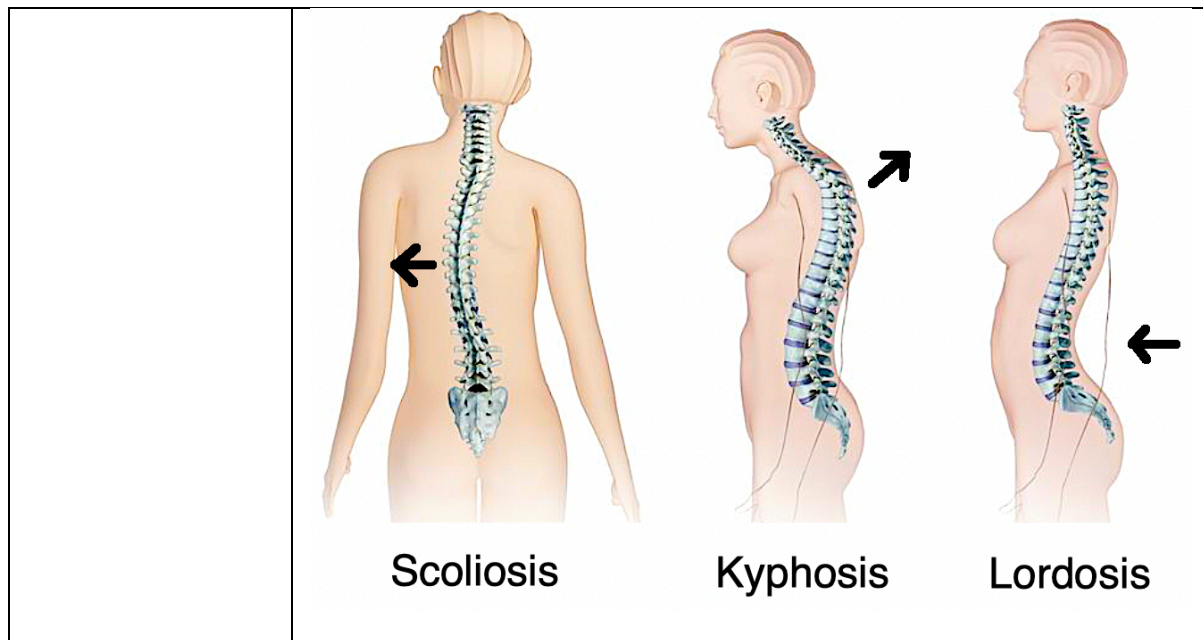
Other upper limb Ddx for Surg	
deQuervain tenosynovitis	<ul style="list-style-type: none"> - Tenosynovitis means inflammation of tendon sheaths. - deQuervain is classic in breastfeeding women and is worsened with Finkelstein test (shown below) → 1) thumb is placed in palm; 2) 2nd-5th fingers are wrapped over the palm; 3) patient ulnar deviates the wrist → this causes pain.  <ul style="list-style-type: none"> - Patient should avoid offending activity, but since this is often breastfeeding, steroid injection can provide immediate relief.
Ganglion cyst	<ul style="list-style-type: none"> - Gelatinous collection of joint fluid; can occur on ankles and flexor areas as well, but classic location is dorsum of hand/wrist.  <ul style="list-style-type: none"> - If Q asks you most likely trajectory if untreated, answer = spontaneous regression. - Tx is needle drainage if disturbing to the patient; recurrence common because the root opening to the tendon sheath is not removed.
Lateral epicondylitis	<ul style="list-style-type: none"> - Tennis elbow. - Lateral elbow pain worsened when patient extends wrist against resistance. - NBME asks “extensor carpi radialis brevis” as answer for site of inflammation. - Tx = “forearm strap” on 2CK forms.
Medial epicondylitis	<ul style="list-style-type: none"> - Golfer elbow. - Medial elbow pain worsened when patient flexes wrist against resistance. - Inflammation at flexor carpi radialis and pronator teres. - Tx = forearm strap.
Radial head subluxation	<ul style="list-style-type: none"> - Aka “nursemaid elbow.” - Child stops using arm + arm pronated and partially flexed. - Hx of child having arm pulled/yanked, or child holding hands and running with older sibling + the child falls, resulting in elbow pull. - Tx = hyper-pronation, OR supination when arm partially flexed. Either is correct. Both will not be listed at the same time as answers.
Olecranon bursitis	<ul style="list-style-type: none"> - Elbow pain, usually following contact injury. - Tx = compression bandage + NSAIDs. Steroid injection is wrong answer on USMLE.

HY MSK spinal conditions for IM	
Cervical spondylosis	 <p>Pars interarticularis</p> <p>Spondylosis (pars interarticularis stress fracture)</p> <ul style="list-style-type: none"> - The answer on USMLE if they say patient over 50 has neck pain + MRI shows degenerative changes of cervical spine. - Can occur in lumbar spine, but USMLE likes cervical spine for this. - Technically defined as degeneration of pars interarticularis component of vertebral body.
Atlantoaxial subluxation	<ul style="list-style-type: none"> - Increased mobility between the first (atlas) and second (axis) vertebrae. - Really HY on 2CK forms patients who have rheumatoid arthritis. - Must do CT or flexion/extension x-rays of cervical spine prior to surgery when a patient will be intubated; I've seen both of these as answers for different Surg Qs. - Q on one of the Neuro CMS forms gives patient with RA not undergoing surgery who has paresthesias of upper limbs → answer is just MRI of cervical spine (implying atlantoaxial subluxation has already occurred).
Lumbar spinal stenosis	<ul style="list-style-type: none"> - Narrowing of the spinal canal. - The answer on USMLE if they mention a patient over 50 who has lower back pain that's worse when walking down a hill (i.e., relieved when leaning forward), or when standing/walking for extended periods of time. - Can cause "neurogenic claudication," where the vignette sounds like the patient has intermittent claudication, but they'll make it clear the peripheral pulses are normal and that the patient doesn't have cardiovascular disease; this shows up in particular on 2CK Neuro CMS forms. - Technically an osteoarthritic change of the spine; therefore increased risk in obesity (but not mandatory for questions).  <p>Normal</p> <p>Spinal stenosis</p>
Cervical foraminal stenosis	<ul style="list-style-type: none"> - The answer on USMLE if they say old woman has difficulty fastening buttons + weakness of hand muscles + loss of sensation of little finger → answer = "C7-T1 foraminal stenosis" (offline NBME 20). - Not stenosis of cervical spinal canal, but stenosis of foramen where nerve exits.

	 <p>Foraminal stenosis</p>
Spondylolisthesis	 <p>Normally aligned vertebrae</p> <p>Spondylolisthesis</p> <ul style="list-style-type: none"> - The answer on USMLE if they a “step-off” between infra-/suprajacent vertebrae. In other words, they’ll say one vertebra “juts out” or has a “step-off” compared to those above/below it. - Can be due to trauma or idiopathic development.
Disc herniation	 <p>Spinal cord</p> <p>Nucleus pulposus</p> <p>Annulus fibrosis</p> <p>Compressed nerve root</p> <p>Vertebral body</p> <ul style="list-style-type: none"> - Herniation of nucleus pulposus through a tear in annulus fibrosis. - The answer on USMLE if they mention radiculopathy (i.e., shooting pain down a leg) after lifting a heavy weight or bending over (e.g., while gardening). They can write the answer as “herniated nucleus pulposus.” - As I mentioned with the radiculopathies above, be aware of the L4, L5, and S1 differences. - Be aware that cervical disc herniation “is a thing,” meaning it’s possible and also assessed on USMLE. 2CK forms ask this a couple times, where patient has shooting pain down an arm, and answer is “C8 disc herniation.”

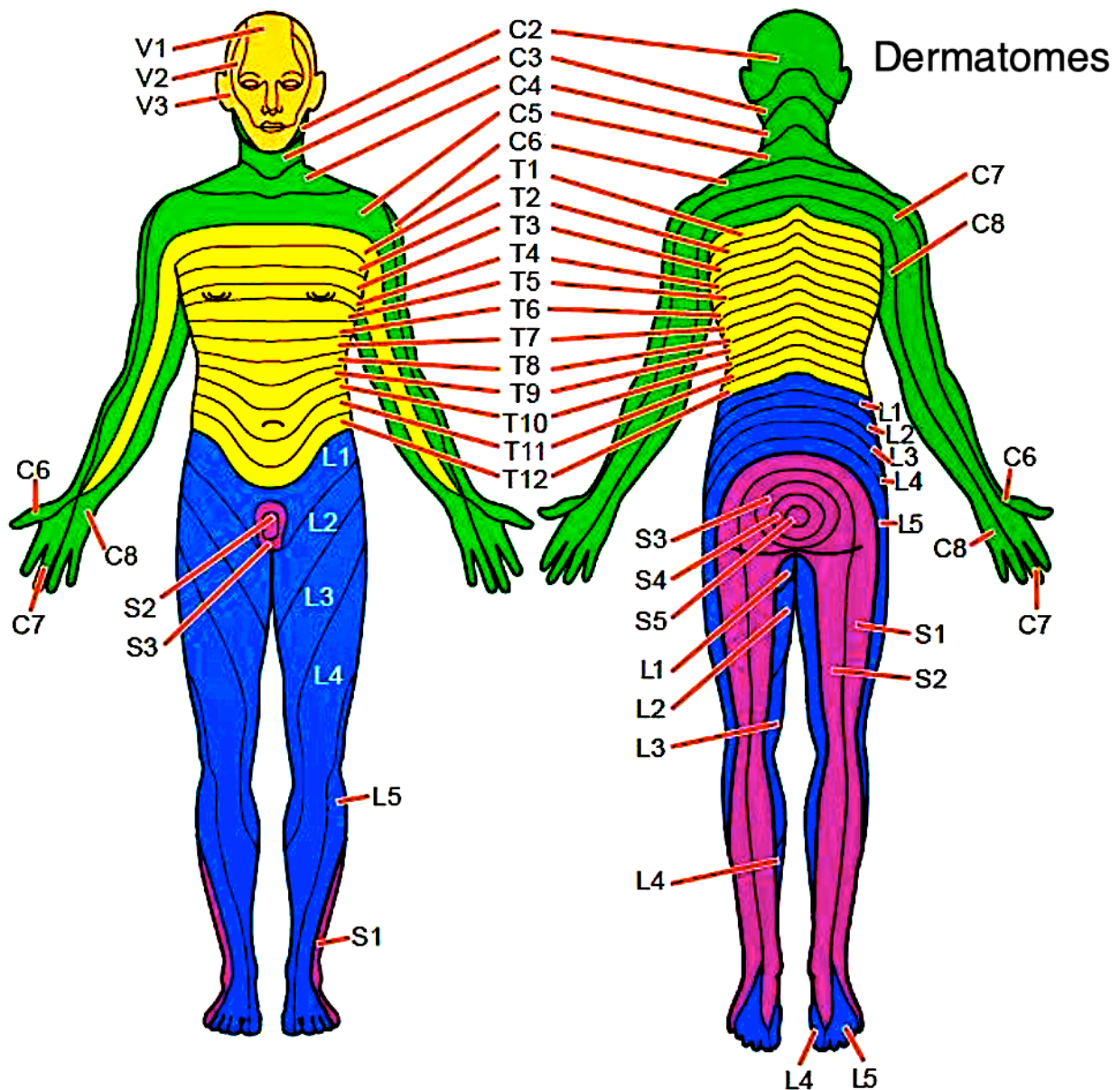
	<ul style="list-style-type: none"> - If suspected, newest NBMEs want “no diagnostic studies indicated.” X-ray and MRI are not indicated unless there is motor/sensory abnormality (i.e., weakness or numbness). But for mere radiculopathy (i.e., radiating pain), no imaging necessary on new NBME content. - Straight-leg raise test is not reliable. Mere pain alone is a negative test. The test is only positive when they say it reproduces radiculopathy/radiating pain. There is a 2CK Q where they say straight-leg test causes pain (i.e., negative test) and answer is “no further management indicated” (i.e., Dx is only lumbosacral strain). - Tx is NSAIDs + light exercise as tolerated. Bed rest is wrong answer on USMLE.
Lumbosacral strain	<ul style="list-style-type: none"> - The answer on USMLE if they say patient has paraspinal muscle spasm following lifting of heavy box without radiculopathy. If they say radiculopathy, the answer is disc herniation instead. - Straight-leg test can cause pain (i.e., negative test). The test is only positive if they it reproduces radiating pain. - Do not x-ray. This is really HY for 2CK. Apparently lumbar spinal x-rays are one of the most frivolously ordered tests, and USMLE wants you to know that you do not order one for simple lumbosacral strain. - Tx is NSAIDs + light exercise as tolerated. Bed rest is wrong answer on USMLE.
Sciatica	<p>- 90% of the time is due to disc herniation.</p>  <p>Sciatica is usually caused by bulging or herniated disc</p> <ul style="list-style-type: none"> - Straight-leg test classically (+) – i.e., reproduces radiating pain. - Tx = Light exercise as tolerated + NSAIDs. Bed rest is wrong answer on USMLE. - On one of the 2CK CMS forms, ibuprofen straight-up is listed as the answer.
Meralgia paresthetica	<ul style="list-style-type: none"> - The answer on USMLE if they say patient has pain or paresthesias running down the lateral thigh. - Due to entrapment of lateral femoral cutaneous nerve. - Often seen as incorrect answer choice on Step, so at least be aware of it.

	 <p>Lateral femoral cutaneous nerve</p> <p>Posterior branch</p> <p>Anterior branch</p> <p>Area of pain</p>
Scoliosis	<ul style="list-style-type: none"> - Sideways curvature of spine, creating an S- or C-shaped curve. - Usually idiopathic; affects 3% of population; girls 4:1.  <p>Normal Spine</p> <p>Scoliosis Rib Rotation</p> <p>Scoliosis X-Ray with Rib Rotation</p> <ul style="list-style-type: none"> - Can be associated with Marfan syndrome, Friedreich ataxia, NF1. - Adams forward bend test used to diagnose. - USMLE wants you to know most children do not need treatment, but that curvatures will remain throughout life. - Answer = bracing if curvature is >25 degrees and child is still growing. - I've never seen surgery as answer for scoliosis on NBME; literature says recommended only when curvature >40 degrees.
Kyphosis	<ul style="list-style-type: none"> - Abnormal convex curvature of thoracic spine. - Usually idiopathic due to old age; can be due to degenerative disc disease and compression fractures (osteoporosis). - If severe, can in theory cause restrictive lung disease due to impaired chest wall expansion.



Lower limb nerve HY Points for IM	
Common peroneal (fibular) nerve	<ul style="list-style-type: none"> - The answer on USMLE if patient loses both eversion and dorsiflexion of the foot. - Sensation to upper third of lateral leg (around and below lateral knee). - Splits into superficial and deep peroneal (fibular) nerves.
Superficial peroneal nerve	<ul style="list-style-type: none"> - The answer on USMLE if patient loses only eversion of the foot, but dorsiflexion stays intact. - Sensation to lower lateral leg and dorsum of foot.
Deep peroneal nerve	<ul style="list-style-type: none"> - The answer on USMLE if patient only loses dorsiflexion of the foot, but eversion stays intact. - Deep for Dorsiflexion, which means superficial is the one that does eversion instead. - Loss of dorsiflexion causes a high-steppage gait (patient has to lift foot high into the air with each step). - Also does sensation to webbing between 1st and 2nd toes. I've never seen NBME Qs ask or give a fuck about this sensation detail, but students get fanatical about it as if it's supposed to be high-yield.
Tibial nerve	<ul style="list-style-type: none"> - The answer on USMLE if patient loses plantarflexion of the foot (can't stand on tippytoes). - Sensation to bottom of foot / heel.
Sciatic nerve	<ul style="list-style-type: none"> - The answer on USMLE if patient has motor dysfunction of tibial and common peroneal nerves at the same time, or has sciatica (shooting pain down leg). - Splits into the common peroneal nerve and tibial nerve. - Does not supply sensation to thigh; sensation encompasses that supplied by the combination of the common peroneal nerve and tibial nerves. - Supplies some motor function to muscles of thigh but USMLE doesn't care. - Sciatica = shooting pain from the lower back down the leg usually as the result of disc herniation; 2CK forms simply want NSAIDs as treatment; straight-leg test is classically used in part to diagnose, but I've seen this test show up on NBME material for simple lumbosacral strain (i.e., the test is non-specific and not reliable).
Obturator nerve	<ul style="list-style-type: none"> - The answer on USMLE if patient has inability to adduct the hip with loss of sensation to medial thigh.
Femoral nerve	<ul style="list-style-type: none"> - The answer on USMLE if patient cannot extend knee and/or has buckling at the knee.

	- Also does sensation to anterior thigh + medial leg (not thigh), although I haven't seen sensation specifically asked for femoral nerve.
Saphenous nerve	- The answer on USMLE if patient loses sensation to medial leg. - Pure sensory branch of the femoral nerve.
Sural nerve	- The answer on USMLE if patient loses sensation to lower lateral leg. In contrast, if sensation loss is upper lateral leg, that's common peroneal nerve instead. - Often confused with saphenous. Good way to remember is: sural is lateral, therefore saphenous must be the one that's medial.
Superior gluteal nerve	- The answer on USMLE if patient has Trendelenburg gait → opposite side of pelvis will fall while walking, so patient will tilt trunk toward side of lesion while walking to maintain level pelvis. - Innervates gluteus medius and minimus.
Inferior gluteal nerve	- The answer on USMLE if patient cannot squat, stand up from a chair, or go up/down stairs. - Innervates gluteus maximus.



Lower limb reflexes / radiculopathies	
L4 radiculopathy	<ul style="list-style-type: none"> - The answer on USMLE if patient loses knee (patellar) reflex + has weakened knee extension. - Pain / paresthesias / numbness in L4 distribution (anterior thigh + medial leg). - Disc herniation of L3-4. - Just remember that L4 is the one where the knee reflex is fucked up.
L5 radiculopathy	<ul style="list-style-type: none"> - The answer on USMLE if patient loses dorsiflexion. - Pain / paresthesias / numbness in L5 distribution (lateral + anterior leg). - Disc herniation of L4-L5.
S1 radiculopathy	<ul style="list-style-type: none"> - The answer on USMLE if patient loses ankle (Achilles) reflex + has weakened plantar flexion. - Pain / paresthesias / numbness in S1 distribution (sole of foot + lower leg). - Disc herniation of L5-S1. - Just remember that S1 is the one where the ankle reflex is fucked up. - SALT → S1, Achilles, Lateral leg dermatome, Tibial motor issue (plantar flexion).

Lower limb DDX for IM	
Trochanteric bursitis	<ul style="list-style-type: none"> - Vignette will be lateral hip pain that is worsened with palpation + lying on one's side in bed. - Tx = NSAIDs.
Septic bursitis	<ul style="list-style-type: none"> - USMLE will give inflammation of knee joint that sounds like septic arthritis, but they will say there's no joint effusion. This is how it presents in a 2CK NBME vignette, where students constantly ask "why not septic arthritis?" And they say in the vignette there's no joint effusion. - Tx = antibiotics.
Prepatellar bursitis	<ul style="list-style-type: none"> - Aka housemaid's knee; presents as anterior knee pain in people who are frequently on their knees (painters, plumbers, etc.). - Tx = NSAIDs.
Patellar tendonitis ("Jumper's knee")	<ul style="list-style-type: none"> - Inflammation of patellar tendon. - The answer on USMLE if they describe anterior knee pain that initially occurs only after finishing sports (e.g., basketball game), then progresses to more chronic pain. - Tx on NBME = "quadricep strengthening exercises."
Patellofemoral instability	<ul style="list-style-type: none"> - Presentation is annoyingly similar to patellar tendonitis, but do not confuse. - Patellofemoral instability is misalignment of the patella at the trochlear groove of the femur. - Q can mention crepitus. - Shows up on 2CK form as teenage girl who has knee pain worse after jumping or running + has crepitus → answer = "patellofemoral instability" (patellar tendonitis / "jumper's knee" not listed as answer).
Patellofemoral pain syndrome	<ul style="list-style-type: none"> - Aka chondromalacia patellae; name implies softening of cartilage in the knee. - The answer on NBME if they say pain that worsens when sitting for long periods of time, or when going up or down stairs. - Classic in obesity or those who squat heavy weight (knees think you're obese). - Tx = quadriceps strengthening exercises.
Anterior cruciate ligament injury	<ul style="list-style-type: none"> - ACL is answer if (+) anterior drawer test or Lachman test → excessive anterior displacement of tibia relative to femur. - Classically injured when knee is hyper-extended, or with a rotational force on a fixed, planted knee.
Posterior cruciate ligament injury	<ul style="list-style-type: none"> - PCL is answer if (+) posterior drawer test → excessive posterior displacement of tibia relative to femur. - Classically injured when knee hits the dashboard in car accident.
Lateral collateral ligament injury	<ul style="list-style-type: none"> - LCL is the answer if varus test induces excessive lateral motion of the knee compared to the unaffected side.

	- Varus test = hand placed on medial knee and pushing outward + other hand placed on lateral ankle and pushing inward.
Medial collateral ligament injury	- MCL is the answer if valgus test induces excessive medial motion of the knee compared to the unaffected side. - Valgus test = hand placed on lateral knee and pushing inward + other hand placed on medial ankle and pulling outward.
Lateral meniscal tear	- Lateral knee pain where patient experiences “locking” or “catching” of the knee in partial flexion. - Diagnosed with McMurray test → internal rotation of leg with concurrent knee extension causes lateral knee pain / “catching.”
Medial meniscal tear	- Medial knee pain where patient experiences “locking” or “catching” of the knee in partial flexion. - Diagnosed with McMurray test → external rotation of leg with concurrent knee extension causes medial knee pain / “catching.”
“Unhappy triad”	- Refers to a trio injury of the ACL, medial collateral ligament, and either the medial or lateral meniscus. - Students are sometimes fanatical about this triad as though it has yieldness. USMLE doesn’t give a fuck. I cannot recall a single NBME question that has ever assessed this. This Dx primarily resides within the domain of Qbank, not the NBME.
Pes anserine bursitis	- The answer on USMLE if patient has inferomedial knee pain.
Iliotibial band syndrome	- The answer on USMLE if they say lateral knee pain, usually in a runner. - Iliotibial band runs from the hip to the knee. Pain may occur anywhere along the hip, lateral thigh, and lateral knee, but is worst in the latter. Tx = conservative with physiotherapy; NSAIDs for pain.
Osgood-Schlatter disease	- Buzzy vignette is knee pain in fast-growing teenage male who plays soccer. Don’t pigeon-hole things, but that’s classic vignette. - Inflammation of the patellar ligament at the tibial tuberosity. - Mechanism is repeated stress on the growth plate of the superior tibia.
Plantar fasciitis	- The answer on USMLE if they give severe heel pain that is worst when first getting out of bed in the morning.
Morton neuroma	- The answer on USMLE if patient has pain + abnormal growth occurring between the 2 nd and 3 rd metatarsals, usually worsened with high-heel shoes. - Benign growth/tumor of intertarsal nerve; cause is idiopathic. - First step in diagnosis is x-ray to rule out arthritis + fractures. Ultrasound is then done to confirm Dx, which will show thickening of interdigital/intertarsal nerve. - Tx = orthotics (comfortable shoes) + steroid injection.
Neurogenic joint	- As discussed already, aka Charcot joint, where patient injures joint due to lack of joint sensation from peripheral neuropathy. - Usually seen in diabetes; can also be seen in neurosyphilis. - The answer on USMLE when they say diabetic patient has “disorganization of the tarsometatarsal joints” on foot x-ray.

HY Fracture points for Surg	
Spiral fracture	- Pathognomonic for child abuse. - Caused by rotational/twisting force applied to a limb. - USMLE doesn’t expect you to diagnose based on imaging.
Simple fracture	- Aka closed fracture – i.e., the skin is not broken and the underlying bone does not pierce the skin.
Compound fracture	- Aka open fracture – i.e., the skin is broken and the underlying bone pierces the skin.
Comminuted fracture	- Fracture where the bone is broken in at least two pieces.
Greenstick fracture	- Bone bends and cracks instead of breaking completely into two pieces. - More common in Peds than adults.

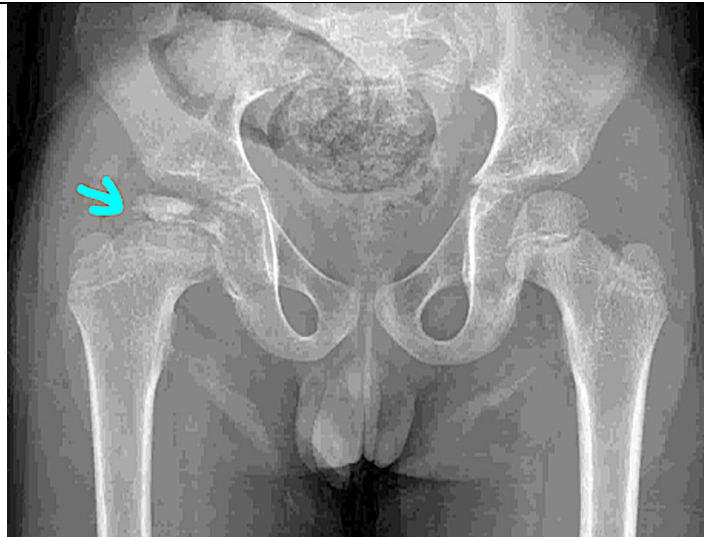
	<ul style="list-style-type: none"> - Children's bones are more flexible than adult bones adults' bones because they have ↑ collagen content and ↓ mineral content, allowing them to bend more. - When a force that would cause a complete fracture in an adult bone is applied to a child's bone, it might only cause a greenstick fracture, which is an incomplete fracture with the bone bending and breaking only on one side, resembling a green branch of a tree that bends and splinters on one side without breaking completely.
Linear skull fracture	<ul style="list-style-type: none"> - Most common type of skull fracture, where there is a break in the skull but the bone has not moved. - USMLE wants you to know this is classically associated with epidural hematoma (asked on 2CK CMS form).
Base of skull fracture	<ul style="list-style-type: none"> - Presents with tetrad of Battle sign (bruising over mastoid process), raccoon eyes (bruising around the eyes), rhinorrhea, and otorrhea.
Metatarsal stress fracture	<ul style="list-style-type: none"> - The answer on USMLE for pain in the metatarsal area of the foot in long-distance runners with low BMI. - Rather than asking diagnosis directly, USMLE will often give a vignette where a female long-distance runner with low BMI already has a metatarsal stress fracture, and then they'll ask what she's at greatest risk of developing → answer = osteoporosis.
Clavicular fracture	<ul style="list-style-type: none"> - Occurs with fall on outstretched hand (FOSH), or occasionally as a result of handlebar injury / impaction, with force transferred up to clavicle. - Most common site of break is the middle-third of the clavicle. - Tx = Figure-of-8 sling.
Scaphoid fracture	<ul style="list-style-type: none"> - As discussed earlier, will present as pain over anatomic snuffbox in patient with FOSH. - X-ray will usually be negative acutely. Must do thumb-spica cast to prevent avascular necrosis of scaphoid, followed by repeat x-ray in 2-3 weeks.
Lunate fracture	<ul style="list-style-type: none"> - The answer on USMLE if FOSH with pain in central palm + no pain over anatomic snuffbox.
Hook of hamate fracture	<ul style="list-style-type: none"> - Cause of distal ulnar nerve injury / Guyon canal syndrome. - Often from handlebar injury / impaction.
Surgical neck of humerus fracture	<ul style="list-style-type: none"> - Causes axillary nerve injury → loss of deltoid function + sensation over deltoid.
Midshaft fracture of humerus	<ul style="list-style-type: none"> - Causes radial nerve injury → wrist-drop + pronated arm.
Supracondylar fracture of humerus	<ul style="list-style-type: none"> - Aka "distal shaft fracture." - Causes median nerve injury → motor/sensory dysfunction of forearm muscles, first three fingers and thenar region.
Vertebral compression fracture	<ul style="list-style-type: none"> - Synonymous with osteoporosis on USMLE (i.e., post-menopausal, corticosteroid-use, Cushing syndrome). - Will often give point tenderness over a vertebra.
Pseudofracture	<ul style="list-style-type: none"> - Band of low-density bone that looks like fracture on x-ray but not actual fracture. - Synonymous with vitamin D deficiency (osteomalacia/rickets) on USMLE. - Can be seen in renal failure, since 1,25-D3 is low. Osteomalacia due to renal failure is called renal osteodystrophy.
Orbital floor fracture	<ul style="list-style-type: none"> - USMLE wants you to know this can cause entrapment of inferior rectus and inferior oblique muscles. - Vignette will say guy got hit in eye by baseball + has impaired upward gaze. - I talk about extraocular muscles and lesions in my neuroanatomy document, but this is one notable point you should be aware of here.

Ottawa criteria

- Used to assess probability of ankle fracture and tells us whether we need to order an X-ray or vs supportive care, e.g., RICE (rest, ice, compression, elevation). Before development of this criteria, x-rays for the ankle used to be ordered frivolously, with most showing no fracture.
- Only order an x-ray for the ankle if:
 - Pain in the malleolar zone, AND any of the following:
 - Tenderness **posterior** to the lateral or medial malleolus; OR
 - Tenderness on the tip of the lateral or medial malleolus; OR
 - Patient cannot bear weight when walking four steps.
- The above might seem nitpicky and pedantic, but this is HY for 2CK. Examples:
- 25M + twisted ankle yesterday + moderate edema of lateral side of ankle with ecchymoses + tenderness to palpation lateral and anterior to lateral malleolus + patient can weight-bear; Q asks, in addition to 2-day ice pack application, what is next best step? → answer on shelf = “use a soft protective brace and early range of motion exercises”; wrong answer = “x-ray of the ankle to rule out fracture.”
- 40M + playing basketball + rolls ankle + pain anterior to lateral malleolus + swelling of ankle + no pain posterior to lateral malleolus + patient can bear weight; Q wants next best step in management → answer = rest, ice, compression, elevation (RICE); wrong answer is x-ray; the patient doesn’t fulfill the Ottawa criteria for x-raying the ankle; he has pain in the malleolar zone but does not have pain posterior to the malleolus or on the tip of the malleolus, and he can bear weight.
- 26F + went running and rolled her ankle + pain in lateral ankle + tenderness posterior to malleolus + can bear weight; Q wants next best step → answer = x-ray of ankle; patient fulfills Ottawa criteria for x-ray → she has pain in malleolar region + tenderness posterior to the malleolus; although she can bear weight, the former two findings satisfy the Ottawa criteria.

HY Pediatric hip disorders for Surg

Primary hip dysplasia	<ul style="list-style-type: none"> - Aka developmental dysplasia of the hip. - Mechanism is “poorly developed acetabulum.” - Initial diagnosis is with Ortolani and Barlow maneuvers, where a “clicking and clunking” is elicited on physical exam. - After the O&A maneuvers, next best step is ortho referral. Sounds wrong, but if it’s listed, it’s the answer before going to imaging. - Definitively diagnose with hip ultrasound if <6 months of age; hip x-ray if >6 months of age. - Treatment is “abduction harness,” aka Pavlik harness, which positions the child’s legs in a frog-leg-appearing manner.
Legg-Calve-Perthes	<ul style="list-style-type: none"> - Aka idiopathic avascular necrosis of the femoral head. - If the etiology for the avascular necrosis is known (i.e., Gaucher, sickle cell, corticosteroids), then the diagnosis is just “avascular necrosis,” not LCP. - Vignette will be child 5-8 years old with hip pain. - First step in diagnosis is hip x-ray, which will show a “contracted” or flattened femoral head. The word “contracted” is HY and synonymous with avascular necrosis. - If x-ray is negative, diagnose with bone scan or MRI (on 2CK form). - Tx = hip replacement.



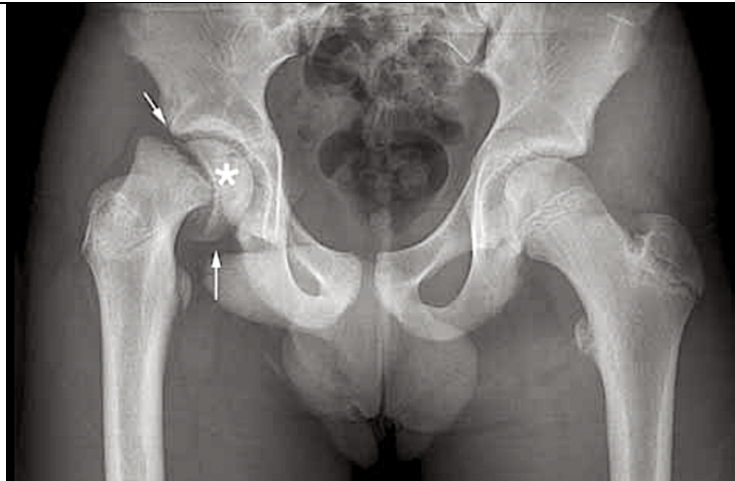
X-ray showing flattened/contracted femoral head (compare with the normal side that looks rounder).



On MRI, the right femoral head (left side of image) appears hypointense (more black). The necrotic / lack of bone in the black superior portion of the femoral head means the remaining white part of the femoral head is “flattened” or “contracted.” The left femoral head (right side of image) shows a small area of necrosis as well (black medial portion).

Slipped capital femoral epiphysis (SCFE)

- Classic vignette is a 10-13-year-old (pre-adolescent) overweight boy with a painful limp.
- NBME will write answer / mechanism as “displacement of the epiphysis of the femoral head.”
- Resources tend to emphasize obesity as the main risk factor, but maybe only ~1/2 of NBME Qs for SCFE give the child as overweight. This causes problems for students, where they rely on seeing high BMI to think SCFE.
- This has led me to conclude that the **age** matters the most, since they will always give a kid who’s about 10-13-ish. If they give you a kid who’s younger, think LCP instead.
- 2CK NBME Q gives 13M with painful gait + no mention of weight → answer is SCFE.
- Another 2CK Q outright says BMI 20 in a 13-year-old who’s 6 feet tall, and answer is SCFE.
- X-ray shows “ice cream falling off the cone.”



X-ray shows the "ice cream slipping off its cone."

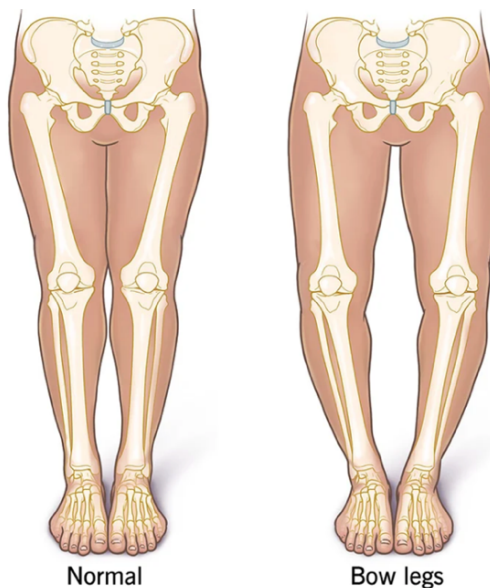
- Offline 2CK gives Q where they say x-ray in 5-year-old shows "contracted capital femoral epiphysis" → answer is LCP, not SCFE. As I said above, "contracted" is HY for LCP. In this case, the younger age + the word "contracted" win over the words "femoral capital epiphysis."

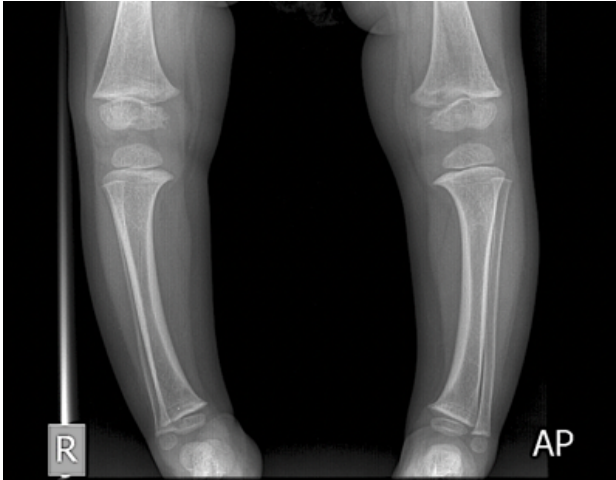

Tx = surgical pinning.

Other Peds bone issues for IM

Rickets

- Rickets = vitamin D deficiency in children. Osteomalacia = vitamin D deficiency in adults.
- Rickets = craniotabes (soft skull), rachitic rosary (bony knobs at costochondral junctions), genu varum (bowing of tibias).
- Activated vitamin D (1,25) is necessary to convert unmineralized osteoid into mineralized hydroxyapatite, therefore hardening bones.
- In both rickets and osteomalacia, patient will have "increased unmineralized osteoid," or "deficient mineralization of osteoid."
- Important cause of Vit D deficiency on USMLE is impaired intestinal malabsorption (i.e., CF, Crohn). For CF, answer can be written as "exocrine pancreas insufficiency."
- "Pseudofracture" on x-ray is buzzy finding in osteomalacia/rickets.
- Patients have $\downarrow \text{Ca}^{2+}$, $\downarrow \text{PO}_4^{3-}$, $\uparrow \text{PTH}$ (due to \downarrow negative feedback at parathyroid glands).



Tibia vara	<p>- Aka Blount disease.</p>  <p>- Bowing of the tibiae after the age of 2 years in a patient whom rickets has been ruled out. - Can be unilateral or bilateral. - Bowing of one or both tibiae is sometimes normal until age 2 years. - Treatment is surgery (osteotomy).</p>
Osteopetrosis	<p>- Osteoclast dysfunction resulting in recurrent fractures in children due to bone density being too high. Sounds weird, but bone strength is based on balanced internal architecture of canals and networks, not just density alone. - HY DDx against osteogenesis imperfecta and child abuse. - Osteoclast dysfunction is due to deficiency of carbonic anhydrase II. This enzyme inside osteoclasts normally allows osteoclasts to form H^+ to resorb bone.</p>
Growing pains	<p>- No, this is not a joke. This is the answer straight-up on a 2CK NBME form. - Vignette is healthy child age 3-12 who awakens from sleep with throbbing pain in the legs. - No treatment necessary. You just need to know this Dx exists and isn't a troll.</p>
Talipes equinovarus	<p>- Aka clubbed foot.</p>  <p>- USMLE just wants you to know that this is treated initially with serial casting. - Usually idiopathic; can be seen in Potter sequence. - Not the same as rocker-bottom foot (aka congenital vertical talus), seen in Edward syndrome.</p>
Arthrogryposis	<p>- You just need to know this is fancy name for a child born with multiple joint contractures. - If they give you a child with not just a clubbed foot, but also knee and/or elbow contractures, etc., the answer is arthrogryposis.</p>

Paget disease

- Idiopathic disorder of increased bone turnover. Bone is described as having mixed osteoblastic and -clastic phases, where bone appears heterogenous on x-ray.
- Buzzy vignette is male over 50 who's hat doesn't fit him anymore + has tinnitus (narrowing of acoustic foramina).
- 19/20 questions will give isolated increase in serum ALP. You need to know Ca^{2+} , PO_4^{3-} , and PTH are all normal in Paget disease. There is one Q on a 2CK CMS form where ALP is given as not elevated, but it's a one-off Q and rare.
- High-output cardiac failure can occur due to intraosseous AV-fistulae, where patient has an S3 heart sound with high, rather than low, ejection fraction.

Osteoporosis



- Bone density >2.5 SD below mean compared to young adult woman. Osteopenia is 1.5-2.5 SD below mean.
- Bone densitometry done at age 65.
- If Q forces you to choose between female gender and age as most important risk factor, choose gender.
- If Q gives you a female and forces you to choose between family history and age, choose family history.
- Males are unlikely to develop osteoporosis, even with family history of females with the disorder.
- If Q gives two women without family history and asks what is most protective against osteoporosis, answer is ethnicity. Black race is protective against osteoporosis.
- If Q gives old woman who has femoral fracture + no mention of osteoporosis in the question, answer = "activity level before fracture" as most important predictor of success in the rehabilitation of the patient → weight-bearing exercise during life is protective against osteoporosis later.
- USMLE loves corticosteroids and Cushing as causes of osteoporosis.
- Compression fractures = osteoporosis on USMLE; e.g., patient with RA on steroids who has compression fracture → easy Dx of osteoporosis.
- Low/low-normal BMI causing osteoporosis is HY; 2CK NBMEs have a couple of nonsense Qs where they give BMI of 19 and 20 in young woman, where they ask what patient is at increased risk of; answer = osteoporosis. Student says, "Wait, but isn't low BMI under 18.5?" I agree. But it's on NBME.
- Metatarsal stress fracture HY in low-BMI young female runners who have low bone density.
- USMLE also is known to assess low vitamin D in the setting of intestinal malabsorption (i.e., CF, Crohn) as cause of osteoporosis, even though that makes no sense, since low Vit D causes osteomalacia.
- Serum calcium, phosphate, PTH, and ALP are all normal in osteoporosis.
- Tx = weight-bearing exercise first (NBME has "go for a long walk outside daily" as correct; wrong answer = "increase participation in swimming pool-based exercise classes to at least three times weekly").
- Calcium and vitamin D are the first medical / pharmacologic treatment.
- Bisphosphonates can be used after Ca^{2+} /VitD.
- Teriparatide is an N-terminus PTH analogue that stimulates bone development.
- Denosumab is a RANK-L monoclonal antibody.

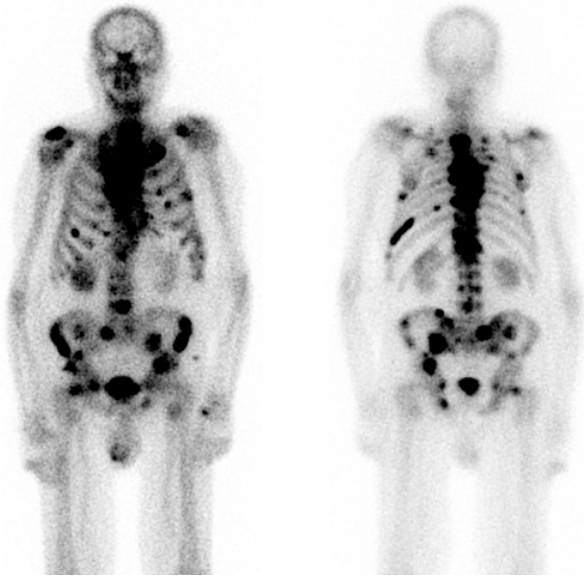
HY bone tumor points for Surg

- I only discuss the ones relevant to Surg shelf.


Osteosarcoma

- Most common primary bone cancer; usually in patients age 10-30.
- *Rb* mutations (congenital retinoblastoma) are associated with osteosarcoma (HY) – i.e., 1-year-old boy has enucleation of eye for retinoblastoma; what is he at risk of developing later in life? → answer = osteosarcoma.
- Can also occur in Paget disease of bone patients (older age).
- Buzzy findings are "Codman triangle" and "Sunburst appearance."
- Codman triangle = periosteal reaction with lifting of periosteum off the bone.
- Sunburst appearance = periosteal reaction described on NBME as "spiculated new born formation."


	 <ul style="list-style-type: none"> - The white arrow is the Codman triangle; the white star is the sunburst appearance. - NBME writes osteosarcoma description as “pleomorphic neoplastic cells producing new woven bone” as correct answer choice.
Unicameral bone cyst	<ul style="list-style-type: none"> - Underrated diagnosis for USMLE. Asked on 2CK exam. - Benign bone tumor that looks similar to osteoclastoma but age of onset usually birth to age 20, rather than 20-40. - Unicameral means “one chamber”; it is fluid-filled.  <p>2CK wants you to know this image for unicameral bone cyst.</p>
Metastases	<ul style="list-style-type: none"> - USMLE loves mets to the vertebrae, particularly from breast, prostate, and lung. - The exam will not show images of spinal cancer mets, but they will give vignette of either lytic lesions of vertebrae in patient with background of cancer, or will give neurologic syndrome (i.e., of cauda equina). - Diffuse bone pain in patient with background of cancer = mets.

	 <p>- Above image shows Technetium-99 bone scan of cancer mets. Similar imaging is on 2CK forms for prostate mets.</p>
--	--

HY myopathies / muscular dystrophies for USMLE	
Duchenne / Becker muscular dystrophy	<ul style="list-style-type: none"> - XR disorder caused by mutation in dystrophin (<i>DMD</i>) gene. - Mutation results in disruption of α-/β-dystroglycan, which is required for proper internal cytoskeletal anchoring of the muscle cell to the extracellular matrix. - Presents with pseudohypertrophy, where muscles appear large but are replaced with fibroadipose tissue (connective tissue stromal cells). - Duchenne presents in a young boy who implements Gower maneuver to stand up (uses arms to walk up off the floor because leg muscles are weak). - Becker presents in adolescence or young adulthood (less severe form of Duchenne). - Duchenne is classically frameshift mutation; Becker is classically not frameshift.
Polymyalgia rheumatica (PMR)	<ul style="list-style-type: none"> - Usually patient over 50 with proximal muscle pain and stiffness. - No weakness on physical exam + creatine kinase (CK) levels are normal. If one or both of these findings is present, the answer is polymyositis, not PMR. - Can present with high ESR and low-grade fever (any autoimmune disease flare can present with low-grade fever). - PMR can present with or without temporal (giant cell) arteritis. Temporal arteritis can present bilaterally on NBME exams; do steroids first to prevent blindness, followed by biopsy second. - Temporal arteritis can cause jaw claudication (pain in the jaw during episodes). In contrast to temporomandibular joint dysfunction (a separate diagnosis), jaw claudication will not be precipitated by eating. - No specific diagnostic test; diagnosis is made clinically. - Tx = steroids. NSAIDs are wrong answer and are not proven to be effective.
Polymyositis / Dermatomyositis	<ul style="list-style-type: none"> - Usually patient over 50 with proximal muscle pain and stiffness. These findings are not unique to PMR. The USMLE will happily give pain and stiffness in polymyositis vignettes. - Key distinction between polymyositis and PMR is that polymyositis will present with 1) muscle weakness on physical exam, and/or 2) increased serum CK. - The muscle weakness *must be on physical exam.* If the patient complains of "weakness" but there is no physical exam findings mentioned in vignette or

	<p>physical exam shows 5/5 strength, there's no weakness. Patients will sometimes mention "weakness," even though they really just have pain and/or stiffness.</p> <ul style="list-style-type: none"> - If polymyositis presents with skin findings, it is called dermatomyositis – i.e., Gottron papules (violaceous papules on the knuckles), mechanics' hands (rough-surfaced hands), shawl rash (body rash), heliotrope rash (violaceous eyelids / periorbital rash; don't confuse with malar rash of SLE). - Patients often positive for anti-Jo1 antibodies. - USMLE wants "electromyography and nerve conduction studies" as first step in management for polymyositis/dermatomyositis. This is what they ask on 2CK NBME forms. I have not seen them ask anti-Jo1 antibodies vs EMG+NCS as two separate answer choices. Usually anti-Jo1 antibodies are mentioned in the vignette rather than as the test you need to order. - Muscle biopsy is confirmatory, showing CD8+ T cell infiltration. The histo can be described as "CD8 + T cells and macrophages surrounding muscle fibers." - For whatever reason, dermatomyositis can be a paraneoplastic syndrome of ovarian cancer (shows up on NBME). <p>Tx = steroids.</p>  <p style="text-align: center;">Gottron papules</p>
Fibromyalgia	<ul style="list-style-type: none"> - This is a psych condition, not an actual muscle disorder, but is often confused with polymyositis and PMR. - Labs will be normal. ESR will not be elevated. Patient will not have fever. - Will be described as woman 20s-50s with multiple (and often symmetric) muscle tenderness points. - Treatment is SSRIs. USMLE can write this as "anti-depressant therapy." This confuses students ("But she doesn't have depression though.") → Right. But SSRIs are still anti-depressant medication.
Temporomandibular joint dysfunction	<ul style="list-style-type: none"> - The answer on USMLE if they give jaw pain that is precipitated by eating. - Often confused with jaw claudication seen in temporal arteritis. In the latter, however, the pain is not precipitated by eating.
Myotonic dystrophy	<ul style="list-style-type: none"> - Autosomal dominant, CTG trinucleotide repeat expansion disease. - Myotonia is inability to relax muscles. - The answer on USMLE if they say patient cannot relax grip on doorknob / handshake, or cannot let go of golf club. - Sometimes associated with early / frontal balding.
Hypothyroid myopathy	<ul style="list-style-type: none"> - Myopathy can occur in both hypo- and hyperthyroidism, yes, but this is especially HY for hypothyroidism on USMLE. - They will often sneak this in as proximal muscle weakness or increased CK in patient who has ongoing fatigue, dysthymia, menstrual irregularities, etc.
Drug-induced myopathy	<ul style="list-style-type: none"> - Classically seen when statins and fibrates are combined, but both drugs can cause myopathy independently. - Mild CK elevations are normal and expected in patients when commencing these agents. Dose does not need to be decreased for mild CK elevations. - USMLE wants "P450-mediated interaction" as the cause of the myopathy when statins and fibrates are combined.

Mitochondrial myopathy	<ul style="list-style-type: none"> - Broad term that can refer to numerous mitochondrial diseases. - USMLE wants you to know the patient has a mitochondrial disorder when he/she presents with hypotonia, ear/eye problems, and lactic acidosis. You want to memorize this tetrad as synonymous with mitochondrial disorders. - "Ragged red fibers" can be a buzzy descriptor in mitochondrial myopathy Qs. - Mitochondrial disorders are maternally inherited only. - Heteroplasmy refers to offspring having varying disease severity based on variation in allocation of diseased mitochondrial genes (I talk more about this stuff in my HY biochemistry PDF).
Inclusion body myositis	<ul style="list-style-type: none"> - The answer if they tell you patient 50 or older has months to years of progressive muscle weakness + biopsy of muscle shows basophilic rimmed vacuoles. - Shows up on a new 2CK form.

Connective tissue disorders	
Marfan	<ul style="list-style-type: none"> - Autosomal dominant; chromosome 15, <i>FBN1/2</i>. - Codes for fibrillin, which is a glycoprotein that forms a sheath around elastin. - Tall, lanky body habitus with flat feet, chest wall abnormalities (i.e., pectus excavatum or carinatum), flat feet (pes planus), scoliosis, mitral valve prolapse (mid-systolic click), increased risk for aortic dissection (can retrograde propagate toward aortic root, causing root dilatation and aortic regurgitation [decrecendo diastolic murmur]). - Is not associated with berry/saccular aneurysms (unlike Ehlers-Danlos and ADPKD).
Ehlers-Danlos	<ul style="list-style-type: none"> - Defect in collagen III synthesis; can be written as "Defect in synthesis of fibrillar collagen." - This can be confusing because fibrillin is completely unrelated and refers to Marfan syndrome. It is just coincidental that "fibrillar collagen" means type III collagen. - Wrong answer = "abnormal synthesis of extracellular glycoprotein" (refers to fibrillin for Marfan syndrome, which as mentioned above, is a glycoprotein that forms a sheath around elastin). - Presents as easy bruising + hyperextensible skin. 
Osteogenesis imperfecta	<ul style="list-style-type: none"> - Collagen I defect that results in recurrent fractures in a child; important DDx are child abuse and osteopetrosis. - Blue sclerae too buzzy and often not mentioned. - Conductive hearing loss due to defective ossicles (middle ear bones). - Many different types of OI, some resulting in miscarriage. Harder vignette can mention child with multiple fractures, where the mom has Hx of recurrent miscarriage.
Mixed connective tissue disease	<ul style="list-style-type: none"> - Answer on USMLE if they give you a patient who has anti-U1-ribonucleoprotein (U1-RNP) antibodies. - Patient presents as having combined features/symptoms from three different disorders → LPS → Lupus, Polymyositis, Scleroderma.

HY neck MSK masses for Surg	
Thyroglossal duct cyst	<ul style="list-style-type: none"> - The answer on USMLE if they say there's a painless, midline neck lump in a child that moves upward with swallowing or protrusion of the tongue. This buzzy description is seen for maybe only about half of Qs. - Can also be described as painless mass inferior to the hyoid bone that demonstrates uptake with a Technetium-99 scan. - USMLE wants "endoderm of foramen cecum" as the embryology.
Sternocleidomastoid injury	<ul style="list-style-type: none"> - The answer on USMLE if they say nodular mass in the lateral neck in an infant who had been born via forceps delivery (risk factor for damage to the muscle).
Branchial cleft cyst	<ul style="list-style-type: none"> - The answer on USMLE if they give idiopathic lateral neck mass in infant that may or may not have an opening to the skin.
Lingual thyroid	<ul style="list-style-type: none"> - Neonates or infants. - Answer for hypothyroidism + a midline neck lump located high in the neck. - They say nothing about protrusion of the tongue or uptake into the mass (of course this is thyroglossal duct cyst instead). - Can sometimes cause dysphagia (trouble swallowing), dysphonia (voice changes), or dyspnea (difficulty breathing).

Highest yield "MSK pharm" for IM	
Alendronate	<ul style="list-style-type: none"> - Bisphosphonate; inhibits osteoclasts. This MOA is HY. - Used for osteoporosis after Ca^{2+}/VitD. - I've seen pamidronate (not alendronate) show up on 2CK forms for Tx of hypercalcemia (after normal saline is given). - Students get fanatical about bisphosphonates causing osteonecrosis of the jaw. The yieldness of this adverse effect is basically non-existent on NBME exams. USMLE wants you to know bisphosphonates cause pill-induced esophagitis. This is very HY for 2CK forms (K^+ supplements also cause esophagitis).
Teriparatide	<ul style="list-style-type: none"> - N-terminus PTH analogue that can induce bone formation. Even though PTH causes bone resorption, this agent stimulates osteoblast-mediated bone formation more than it induces RANK-L-mediated activation of osteoclasts. - Can be used for severe/advanced osteoporosis.
Denosumab	<ul style="list-style-type: none"> - Monoclonal antibody against RANK-L. - Can be used for severe/advanced osteoporosis.
Baclofen	<ul style="list-style-type: none"> - Agonizes GABA_B. - Used for spasticity, classically in multiple sclerosis, but I've seen one NBME Q where it's used for random spasticity in an older dude. - Students frequently remember GABA_B for this drug, but often say "antagonist" when I probe them further. So remember: it's an agonist, not an antagonist, at GABA_B.
Cyclobenzaprine	<ul style="list-style-type: none"> - Muscle relaxant used for spasms. - Structurally similar to TCAs; helps modulate pain sensation at brain stem.
Benzotropine	<ul style="list-style-type: none"> - Muscarinic (cholinergic) receptor antagonist. - Used to treat acute dystonia due to anti-psychotics. - If patient starts anti-psychotic and then gets stiff neck, oculogyric crisis (abnormal eye movements), or muscle rigidity without fever, the answer = benztropine.
Diphenhydramine / Chlorpheniramine	<ul style="list-style-type: none"> - First-generation histamine-1 (H1) antagonists. - Diphenhydramine is quite possibly the highest-yield drug on USMLE. - Used to treat acute dystonia, similar to benztropine, as well as motion sickness. - H1 blockers can treat allergies in theory, but they have nasty anti-cholinergic (anti-muscarinic) side-effects. - The anti-cholinergic side-effects are interestingly a <i>good</i> thing, however, when we want to treat acute dystonia. Psych Qs will either list benztropine or diphenhydramine (or chlorpheniramine) as the answer, but not both at the same time.

	<ul style="list-style-type: none"> - For whatever reason, anti-cholinergic effects treat motion sickness. Scopolamine is an anti-cholinergic used to treat motion sickness classically. But I've seen NBME ask diphenhydramine straight-up for this as well – i.e., the nasty anti-cholinergic side-effects are, once again, a good thing if the aim is Tx of motion sickness. - 1st-gen H1 blockers can cause cognitive dysfunction (delirium, as well as worsening of dementia) and drowsiness. Therefore avoid in elderly and locomotive/machine operators if at all possible. - 1st-gen H1 blockers can also cause anti-α1-adrenergic effects (orthostatic hypotension). - I talk about all of the pharm-related stuff in a lot more detail in my free pharm modules on the website.
Dantrolene	<ul style="list-style-type: none"> - Blocks ryanodine Ca^{2+} channel. - Tx for neuroleptic malignant syndrome (NMS) and malignant hyperthermia (MH). - If patient gets muscle rigidity and fever following commencement of anti-psychotic, or following administration of succinylcholine during surgery, answer = dantrolene. (Bromocriptine for NMS is low-yield and rarely seen on NBME). - NBME will sometimes give vignette of NMS or MH, and then the answer for Tx is “decreases sarcoplasmic calcium release.” - In NMS and MH, the ryanodine channel, which allows calcium to move from the sarcoplasmic reticulum into the cytosol, gets stuck open, so high amounts of calcium moves into the cytoplasm. The cell then needs to use a lot of ATP to pump the calcium back into the sarcoplasmic reticulum. This generates heat → fever. Dantrolene closes this channel.

IM Immuno

Immunodeficiencies HY points for IK	
- 2CK is known to ask immunodeficiency mechanism Qs at "Step 1-level detail."	
Severe-combined immunodeficiency (SCID)	<ul style="list-style-type: none"> - X-linked recessive most common → usually due to common gamma chain mutation, or mutation in IL-2 receptor. - Autosomal recessive type less common → due to deficiency in adenosine deaminase (ADA). - Combined T and B cell deficiency. - T cell deficiency → absent thymic shadow. - B cell deficiency → scanty/absent lymph nodes and tonsils. - Q will give you sick kid who's had infections of all different types (i.e., viral, fungal, bacterial, protozoal) since birth. - This contrasts with Bruton XLA, which will be <i>just</i> bacterial infections (usually since 6 months of age). - Tx = bone marrow transplant.
Bruton X-linked agammaglobulinemia (XLA)	<ul style="list-style-type: none"> - X-linked recessive (as name implies) → caused by mutation in Bruton tyrosine kinase. - Isolated B cell deficiency. - Scanty/absent lymph nodes + tonsils. - Kid will have ↓ immunoglobulins of all classes (because B cells make Ab). - Q will almost always be a boy who's had only bacterial infections since 6 months of age (if they mention bacterial <i>and</i> viral, fungal, and/or protozoal, the Dx is SCID). - There is a Q on a 2CK form where they say "bacterial infections since birth," but you're able to eliminate the other answers (literally 14/15 Qs will say from ~5-7 months-onward, so this is a highly annoying point to have to make, but I have to communicate it because it's on the NBME). - Tx on NBME is "monthly infusion of immunoglobulin." - Answer on USMLE will often be "deficiency of humoral immunity," rather than just "Bruton XLA."
IgA deficiency	<ul style="list-style-type: none"> - One of the highest yield conditions for the Step (hence I mention it repeatedly in this doc; purposeful redundancy). - Most common hereditary immunodeficiency. - 9/10 Qs will give you recurrent sinopulmonary infections in someone between high school and 30s; one 2CK Q has it in a kid; the Q might say the patient has a sore cheek (sinusitis) + Hx of pneumonia. - Anaphylaxis with transfusion of blood products is ultra-HY detail but often omitted from real NBME Qs because it's too easy/buzzy. - Atopy is really HY (asthma, seasonal allergies, eczema). - Hx of Giardia infection. - Associated with other autoimmune diseases (i.e., vitiligo, Celiac). - Celiac Ab screen falsely negative in IgA deficiency. - IgA deficiency can be associated with false-positive pregnancy tests (yes, fucking weird, but due to heterophile Ab production apparently, with zero relation to EBV). - Answer on USMLE will often be "deficiency of mucosal immunoglobulin" or "deficiency of humoral immunity," rather than just "IgA deficiency."
DiGeorge syndrome	<ul style="list-style-type: none"> - T cell deficiency caused by 22q11 deletion. - Failure of development of 3rd and 4th pharyngeal pouches (not arches) → 3rd becomes thymus + two inferior parathyroids (these structures form a triangle → 3rd); 4th becomes two superior parathyroids. - Absent thymic shadow.

	<ul style="list-style-type: none"> - Hypocalcemia due to hypoparathyroidism (positive Chvostek and Trousseau signs of hypocalcemia). - Tetralogy of Fallot (VSD, overriding aorta, pulmonic stenosis, RVH) and truncus arteriosus are HY cardiac anomalies. - Cleft lip/palate may or may not be mentioned. - Patient will have <i>normal</i> antibody levels (even though T cells activate B cells, choose normal Ab levels).
Chronic mucocutaneous candidiasis	<ul style="list-style-type: none"> - T cell dysfunction. - Recurrent candidal skin infections since birth. - Choose "deficiency of cell-mediated immunity." - Associated with other autoimmune diseases (i.e., T1DM, thyroiditis). - 17F + recurrent candidal skin infections since birth + one year Hx of autoimmune thyroiditis + 2-yr Hx of T1DM; mechanism for infections? → answer = "deficiency of cell-mediated immunity."
NADPH oxidase deficiency	<ul style="list-style-type: none"> - Aka chronic granulomatous disease (CGD). - Usually X-linked recessive. - First enzyme of the respiratory burst; converts molecular O₂ → superoxide. - Recurrent infections with catalase (+) organisms: <i>Serratia</i>, <i>Pseudomonas</i>, <i>Aspergillus</i>, <i>Candida</i>, <i>E. coli</i>, <i>Staph</i>, <i>H. pylori</i>. - Condition results in ↓ ability of patient to synthesize enough H₂O₂ to overwhelm catalase (+) organisms. - Diagnose with dihydrorhodamine test (tetrazolium blue assay is atavistic and the wrong answer if both are listed, as per NBME).
Myeloperoxidase (MPO) deficiency	<ul style="list-style-type: none"> - Autosomal recessive. - Last enzyme in respiratory burst; converts H₂O₂ → hydroxyl-halide radicals (bleach). - Q will literally give you a one-liner telling you someone can't produce hydroxyl-halide radicals, and the answer is myeloperoxidase deficiency. - Q can mention myeloperoxidase deficiency in vignette, and then the answer is "impaired conversion of hydrogen peroxide to hypochlorous acid." - Usually presents as mix of <i>Staph aureus</i> and <i>Candida</i> infections. - Q on Free 120 gives mix of <i>S. aureus</i> and <i>Candida</i> infections in 6-year-old girl with AR disorder; Q wants MPO deficiency as answer, not CGD. Even though CGD can present with same organisms, the literature not only says 70% of CGD cases are XR, but if CGD occurs in children, it's usually XR, since less-frequent AR CGD is often more mild and presents later.
Wiskott-Aldrich syndrome	<ul style="list-style-type: none"> - X-linked recessive (WAS gene). - T cell cytoskeletal dysfunction. - Triad of: immunodeficiency, eczematoid skin lesions, thrombocytopenia. - ↑ serum IgA/IgE; ↓ IgM. - 12M + <i>Pneumocystis</i> infection + Hx of nosebleeds + eczema; Q asks what cell is dysfunctional? → answer = T cell. - Answer can be "deficiency of cell-mediated immunity."
Leukocyte adhesion deficiency (LAD)	<ul style="list-style-type: none"> - Deficiency of CD18/LFA-1 integrin. - ↓ ability of leukocytes to leave blood vessels for sites of infection → ↓ pus. - Classically associated with delayed separation of umbilical cord. - Answer can be "defective leukocyte chemotaxis" instead of just "LAD."
Chediak-Higashi syndrome	<ul style="list-style-type: none"> - Phagolysosomal fusion disorder with disruption of microtubule function. - Melanosome function also impaired → partial albinism / fairer skin than siblings. - Giant granules in phagocytes in neutrophils and eosinophils.
Ataxia-telangiectasia	<ul style="list-style-type: none"> - Failure of double-stranded DNA break repair. - Cerebellar atrophy → ataxia. - Telangiectasias. - ↑ susceptibility to radiation → ↑ risk of leukemia and lymphoma.
Hyper-IgM syndrome	<ul style="list-style-type: none"> - Deficiency of CD40L on CD4+ T cells.

	- ↓ activation of CD40 on B cells → ↓ B cell activation → ↓ ability to differentiate into plasma B cells + isotype class-switch → Ab isotype “stuck” at IgM.
Hyper-IgE (Job) syndrome	- FATED → abnormal F acies, staphylococcal cold A bscesses, retained primary T eeth, hyper IgE , D ermatologic findings (e.g., eczematoid lesions).
IL-12 receptor deficiency	- Recurrent TB infections. - Important point for USMLE is that Th1 CD4+ T cells and macrophages activate each other in a cyclical loop via IL-12 and IFN-γ. Th1 cell lacking IL-12 receptor cannot get activated and therefore does not secrete IFN-γ → macrophages not activated → ↓ granuloma formation.
Common variable immunodeficiency (CVID)	- Normal B cell number but defective maturation into plasma cells. - ↓ immunoglobulin production. - Will be the answer if the Q gives you an <i>adult</i> who has had recurrent sinopulmonary infections (similar to IgA deficiency), except ↓ Ig not limited to IgA; in addition, if vignette gives you atopy or Giardia, answer is IgA deficiency not CVID.
Terminal complement deficiency	- Deficiency of C5-C9 complement proteins - Cannot form membrane attack complex (MAC) - Recurrent <i>Neisseria</i> infections (both gonococcal and meningococcal) - Q will often have deficiency of “C7” or “C8” as the answer (i.e., they choose a random terminal complement protein), or “terminal complement deficiency,” or “complement-mediated immunodeficiency”

HY autoantibodies for USMLE	
HY disease association	HY antibodies
Antiphospholipid syndrome	Anti-β2-microglobulin; anti-cardiolipin; lupus anticoagulant (the latter is the name for either of the former two if the patient happens to have SLE); Abs associated with recurrent miscarriage; can cause false-positive syphilis screening (e.g., SLE patient who gets positive syphilis VDRL test)
Bullous pemphigoid	Anti-hemidesmosome (bullous pemphigoid antigen); hemidesmosomes connect the dermis to epidermis; cause a linear immunofluorescence on skin biopsy
Pemphigus vulgaris	Anti-desmosome (anti-desmoglein 1 and 3); desmosomes connect adjacent cells in epidermis; cause a net-like immunofluorescence on skin biopsy
Goodpasture syndrome	Anti-collagen IV (anti-GBM; glomerular basement membrane); causes linear immunofluorescence on renal biopsy; don't confuse with Alport syndrome, which is <i>mutations</i> in type IV collagen (not Ab)
Granulomatosis with polyangiitis (Wegener)	c-ANCA; anti-proteinase 3 (PR3); dumb mnemonic I created that helps some of my students: W ater C loset (W egener C -ANCA)
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)	p-ANCA (anti-myeloperoxidase)
Microscopic polyangiitis	p-ANCA (anti-myeloperoxidase)
Systemic lupus erythematosus (SLE)	Anti-double-stranded DNA (dsDNA); anti-Smith (ribonucleoprotein); anti-hematologic cell line Abs; should be noted that dsDNA goes up in acute flares + best reflects renal prognosis; anti-Smith is <i>more specific</i> than anti-dsDNA; thrombocytopenia is an exceedingly HY finding in SLE due to Abs; if all cell lines are down in SLE, aplastic anemia (↓ bone

	marrow production) is wrong answer; choose "increased peripheral destruction" as answer
Drug-induced lupus (DIL)	Anti-histone; caused by various drugs (Mom is HIPP) → M inocycline, H ydralazine, I NH, P rocainamide, P enicillamine
Myasthenia gravis	Anti-post-synaptic acetylcholine receptor; sometimes a paraneoplastic of thymoma
Lambert-Eaton	Anti-presynaptic voltage-gated calcium channel; sometimes a paraneoplastic of small cell lung cancer
Small cell cerebellar dysfunction	Anti-Hu/-Yo; ataxia in someone with small cell lung cancer and negative CNS imaging
Polymyositis / Dermatomyositis	Anti-Jo1; can be a paraneoplastic of ovarian cancer
Limited-type systemic sclerosis / scleroderma	Anti-centromere
Diffuse-type systemic sclerosis / scleroderma	Anti-topoisomerase I (Scl-70)
Primary biliary cirrhosis	Anti-mitochondrial
Autoimmune hepatitis	Anti-smooth muscle
Rheumatoid arthritis	Rheumatoid factor (an IgM against the Fc region of IgG); anti-cyclic citrullinated peptide (CCP); anti-CCP is <i>more specific</i> than rheumatoid factor
Sjogren syndrome	Anti-SS-A (anti-Ro); anti-SS-B (anti-La)
Graves disease	Anti-TSH receptor (this antibody is called thyroid-stimulating immunoglobulin, or TSI, and <i>activates</i> the TSH receptor)
Hashimoto thyroiditis	Anti-thyroperoxidase (anti-microsomal); anti-thyroglobulin
Pernicious anemia	Anti-parietal cell; anti-intrinsic factor
Celiac disease	Anti-endomysial (aka anti-gliadin); anti-tissue transglutaminase IgA; antibody screening will yield false-negatives if patient also has IgA deficiency
Type I diabetes mellitus	Anti-glutamic acid decarboxylase (anti-GAD); anti-zinc transporter 8
Primary membranous glomerulonephritis	Anti-phospholipase A2 receptor
Thrombotic thrombocytopenic purpura	Anti-ADAMTS13 (a matrix metalloproteinase that cleaves vWF multimers)
Immune thrombocytopenic purpura (aka idiopathic thrombocytopenic purpura)	Anti-GpIIb/IIIa on platelets (platelet aggregation)
Heparin-induced thrombocytopenia (HIT)	Anti-platelet factor 4-heparin complex (anti-PF4-heparin)
Addison disease	Anti-21-hydroxylase
Rheumatic heart disease	Anti-myosin; anti-valve-derived proteins; should be noted that these Abs are formed against <i>S. pyogenes</i> M protein and almost always cross-react with the mitral valve (molecular mimicry)
Neuromyelitis optica (Devic syndrome)	Anti-aquaporin 4 (asked on 2CK form)
Cold autoimmune hemolytic anemia	IgM against RBCs (CMV and <i>Mycoplasma</i> are HY infectious associations); will result in positive Coombs test
Warm autoimmune hemolytic anemia	IgG against RBCs (various miscellaneous drugs and infections); also associated with chronic lymphocytic leukemia; will result in positive Coombs test

IM Biochem

Phakomatoses (neurocutaneous disorders)	
Neurofibromatosis type I (NF1)	<ul style="list-style-type: none"> - <i>NF1</i>; AD; chromosome 17. - Neurofibromas, café au lait spots (hyperpigmented macules), axillary/groin freckling, Lisch nodules (iris hamartomas), pheochromocytoma, optic nerve glioma, oligodendroglioma, ependymoma.
Neurofibromatosis type II (NF2)	<ul style="list-style-type: none"> - <i>NF2</i>; AD; chromosome 22. - In kids, sometimes causes bilateral cataracts. - Bilateral acoustic schwannomas + meningioma in adults.
Tuberous sclerosis (TSC)	<ul style="list-style-type: none"> - <i>TSC1/2</i> genes; AD. - Periventricular nodules (tubers) on MRI of head, seizures, adenoma sebaceum (angiofibromas), subungual fibromas, renal angiomyolipoma, cardiac rhabdomyoma, hypopigmented macules ("ashleaf spots"), hyperpigmented velvety lesions ("shagreen patches").
Von Hippel-Lindau	<ul style="list-style-type: none"> - <i>VHL</i>; AD; chromosome 3. - Cerebellar/retinal hemangioblastomas, bilateral renal cell carcinoma, pancreatic cysts. - Mutation causes constitutive activation of hypoxia-inducible factor.
Sturge-Weber	<ul style="list-style-type: none"> - Not inherited; somatic mosaicism of <i>GNAQ</i> gene. - Port wine stain birth mark (nevus flammeus; may also present as violaceous papules in temporal distribution), leptomeningeal angioma (presenting as seizure); glaucoma.

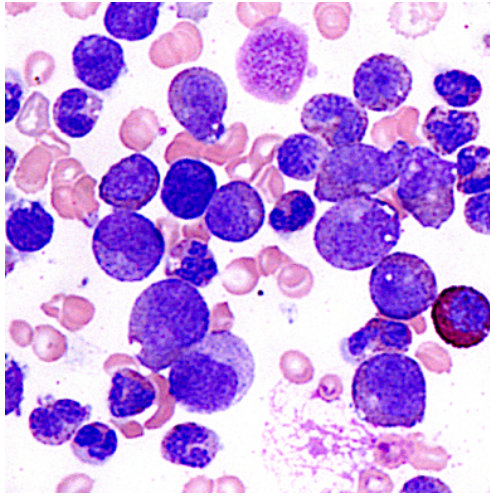
Glycogen storage diseases	
Disease	HY points
Type I (Von Gierke)	<ul style="list-style-type: none"> - Deficiency of glucose-6-phosphatase - Lactic acidosis. - Hypoglycemia, jaundice, hepatomegaly. - "Super sick kid with glycogen storage disease."
Type II (Pompe)	<ul style="list-style-type: none"> - Deficiency of Debranching α1,4-glucosidase (aka lysosomal acid maltase). - Cardiomyopathy, hepatomegaly. - The answer for glycogen storage disease + heart problem."
Type III (Cori)	<ul style="list-style-type: none"> - Deficiency of α1,6-glucosidase (debranching enzyme). - No lactic acidosis (in contrast to von Gierke). - "Not so sick kid with glycogen storage disease."
Type V (McArdle)	<ul style="list-style-type: none"> - Deficiency of myophosphorylase (glycogen muscle phosphorylase). - Patient usually adolescent or adult. - severe cramping/rhabdo after intense exercise, but normal serum lactate.

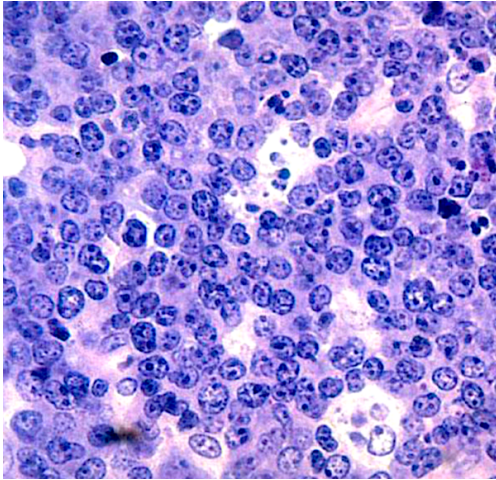
Collagen disorders	
Type I	<ul style="list-style-type: none"> - Found in bone; predominates in late wound healing (white in color); \uparrow tensile strength than type III. - Osteogenesis imperfecta \rightarrow fractures at different stages of healing; often mistaken for child abuse; blue sclerae (too easy; often omitted from Qs); conductive hearing loss (malformation of ossicles); if ruled out OI + child abuse, think osteopetrosis.
Type II	<ul style="list-style-type: none"> - Found in cartilage, intervertebral discs, and vitreous humor. - Stickler syndrome \rightarrow congenital hearing loss.
Type III	<ul style="list-style-type: none"> - Found in blood vessels; early wound healing (pink in color); \downarrow tensile strength compared to type I.

	- Ehlers-Danlos (vascular type) → hyperextensible skin/joints; easy bruising; aortic dissection/regurgitation; mitral valve prolapse (myxomatous degeneration); circle of Willis berry (saccular) aneurysms.
Type IV	- Found in basement membranes of the kidney + alveoli; also found in the lens, cornea, and inner ear. - Alport (XR; <i>mutation in type IV collagen</i>); eye/ear problems in male with hematuria. - Goodpasture (<i>Abs against type IV collagen</i>); male 20s-40s with hemoptysis + hematuria; linear immunofluorescence pattern on biopsy.

Lysosomal storage diseases			
- All are associated with cognitive/neurologic deficits. - AR except for Fabry and Hunter, which are XR.			
Disease	Enzyme deficiency	Buildup product(s)	HY points
I-cell	N-acetylglucosamine-1-phosphotransferase	Many lysosomal enzymes	- Cannot synthesize mannose-6-phosphate at the Golgi; M6P needed to target lysosomal enzymes to the lysosomes; instead, lysosomal enzymes are secreted into cytosol + serum. - Coarse facial features, joint contractures, hepatomegaly, recurrent ear infections.
Gaucher	Glucocerebrosidase	Glucocerebroside	- Avascular necrosis of the hip. - "Crumpled tissue paper" (i.e., lipid-laden) macrophages. - The answer if they give you lysosomal storage disease + a bone problem.
Tay-Sachs	Hexosaminidase A	GM2 ganglioside	- Cherry red spot on macula (blindness). - No hepatosplenomegaly. - Neurodegeneration.
Niemann-Pick	Sphingomyelinase	Sphingomyelin	- Cherry red spot on macula (blindness). - Yes, hepatosplenomegaly. - Niemann-Pick is a longer name than Tay-Sachs, and hepatosplenomegaly is a long word, so Niemann-Pick is the one with HSM. - Neurodegeneration.
Metachromatic leukodystrophy	Arylsulfatase A	Cerebroside sulfate	- Progressive neurologic decline.
Krabbe	Galactocerebrosidase	Galactocerebroside, psychosine	- Aka Globoid cell leukodystrophy. - Globoid cells (giant, multinucleated cells). - Neurodegeneration.
Fabry (XR)	α -galactosidase A	Ceramide trihexoside	- Angiokeratomas (small, red/purple dots on the skin due to capillary dilation). - Heart and/or renal problems.
Hunter (XR)	Iduronate sulfatase	Glycosaminoglycans (GAGs) – i.e., Dermatan + heparan sulfates	- Gargoyle-like facies, stridor, aggressive behavior. - No clouded corneas. - "Hunters can see the X" → Therefore XR and no clouded corneas.
Hurler	α -L-iduronidase		- Gargoyle-like facies, stridor, aggressive behavior. - Yes, clouded corneas. - More severe form of Hunter.

IM Gen Path

HY Cancer Genes	
<i>APC</i>	<ul style="list-style-type: none"> - Mutations cause Familial Adenomatous Polyposis (FAP); chromosome 5; AD. - Hundreds to thousands of polyps on colonoscopy; 100% cancer risk. - Answer on 2CK form is total proctocolectomy in 18-year-old (presumably since 100% chance of cancer + too difficult to conservatively screen). - FAP + soft tissue (e.g., lipoma) or bone tumors (e.g., of the skull) = Gardner syndrome. - FAP + CNS tumors = Turcot syndrome.
<i>BCL-2</i>	<ul style="list-style-type: none"> - Overexpressed in follicular lymphoma (most common indolent non-Hodgkin lymphoma) as a t(14;18) translocation. - Codes for anti-apoptotic molecule. - Follicular lymphoma will present as waxing/waning painless lateral neck mass over 1-2 years in an adult. - USMLE might give research-type Q where <i>BCL-2</i> is overexpressed (unrelated to follicular lymphoma) and they ask what would be expected → answer = increased lifespan of population of cells (makes sense, since anti-apoptotic molecule).
<i>BCR-ABL</i>	<ul style="list-style-type: none"> - HY for chronic myelogenous leukemia (CML). - t(9;22) translocation of these two genes (aka Philadelphia chromosome) codes for a "fusion protein." - This fusion protein = an oncogenic tyrosine kinase. - CML is answer for leukemia when the Q gives you lots of myelo-sounding cells (i.e., myelocytes, promyelocytes, metamyelocytes). 4/5 Qs on USMLE that mention these cells are CML. Leukocyte ALP will be low.  <ul style="list-style-type: none"> - The blood smear for CML I refer to as a "motley mix," or a "soup." This is a buzzy image on NBME for CML. - Imatinib is Tx for CML. It can cause fluid retention / peripheral edema. - The MOA of imatinib = targets <i>BCR-ABL</i> tyrosine kinase.
<i>BRAF</i>	<ul style="list-style-type: none"> - Proto-oncogene that can be seen in some melanomas. - Codes for serine-threonine kinase.
<i>BRCA1/2</i>	<ul style="list-style-type: none"> - Breast cancer tumor suppressor genes. - NBME exam asks for what the gene does → answer = "recombinational ds-DNA repair." - Can also lead to gynecologic cancers in females or breast/testicular cancers in males. - Answer on an NBME exam for appropriate prophylaxis in patient who has confirmed mutation is "bilateral oophorectomy and mastectomy."
<i>c-KIT</i>	<ul style="list-style-type: none"> - Proto-oncogene; can be mutated in some gastrointestinal stromal tumors (GIST).
<i>c-MYC</i>	<ul style="list-style-type: none"> - Overexpressed in Burkitt lymphoma (a type of NHL) as a t(8;14) translocation. - Codes for a transcription factor.

	<ul style="list-style-type: none"> - Burkitt lymphoma will be mass of the jaw or abdomen. - Histo is buzzy for “starry sky” appearance, which is a basophilic (purple) background of B cells with scattered translucent macrophages.  <ul style="list-style-type: none"> - The macrophages are referred to as “tingible body” macrophages (correct, not tangible), where apoptosis occurs. This is asked on an NBME exam, where they have an arrow that points to one of the macrophages, and the answer is apoptosis.
<i>EGFR</i>	<ul style="list-style-type: none"> - Non-small cell lung cancer (adenocarcinoma) and glioblastoma multiforme. - Codes for EGFR tyrosine kinase. - Erlotinib asked on USMLE → targets EGFR tyrosine kinase.
<i>HER2/neu (ERBB2)</i>	<ul style="list-style-type: none"> - Tyrosine kinase expressed in some breast cancers. If (+) → poor prognostic indicator. - Trastuzumab (Herceptin) is a drug that targets <i>HER2/neu</i>. It can cause cardiotoxicity.
<i>JAK2</i>	<ul style="list-style-type: none"> - Can be activated in polycythemia vera, essential thrombocytosis, and myelofibrosis. - USMLE wants increased proliferation of hematopoietic stem cells, not pluripotent stem cells, for PV. Patient will have high RBCs, PLUS either high WBCs and/or platelets (i.e., 2-3 of the cell lines will be high in Qs, but RBCs are always high). Generalized pruritis after showers can be seen from basophilia. Hyperviscosity syndrome (i.e., blurry vision, headache, Raynaud) from high RBCs is treated with phlebotomy. Hydroxyurea can decrease recurrence of episodes. - Essential thrombocytosis will present in Qs as platelets over a million (NR 150-450,000). They will say there’s pain or discoloration in tips of fingers or give hyperviscosity-type findings. Bone marrow will show increased megakaryocytic proliferation (this latter finding will not be seen in reactive thrombocytosis, which is high platelets from infection). - Myelofibrosis will present with teardrop-shaped RBCs (dacrocytes) and/or “dry tap” on bone marrow aspiration. Massive splenomegaly is seen in basically all questions.
<i>KRAS</i>	<ul style="list-style-type: none"> - Proto-oncogene; codes for a GTPase. - The answer on USMLE for the first gene mutated in colonic polyps, prior to progression to overt colon cancer. - Colon cancer often develops as a result of <i>progressive</i> mutations, rather than one mutation straight-up. In other words, first <i>KRAS</i>, then <i>PTEN</i>, then <i>DCC</i>, then <i>TP53</i>. - If they tell you a colon cancer has metastasized and force you to choose a gene that’s mutated, go with <i>TP53</i> (codes for p53 protein). - If they tell you a polyp is seen and there is no evidence of invasion of the stalk, choose <i>KRAS</i>. This is on NBME exam.
<i>MEN1</i>	<ul style="list-style-type: none"> - Mutations cause Multiple Endocrine Neoplasia type I. - 3Ps → Pituitary tumor (e.g., prolactinoma), Parathyroid adenoma (or diffuse 4-gland hyperplasia), and Pancreatic tumor (e.g., gastrinoma; Zollinger-Ellison syndrome). - HY point is that NBME Qs need not give all findings within a MEN syndrome. For example, the Q can give gastrinoma alone and ask for the gene → <i>MEN1</i>.
<i>MSH2/6</i> <i>MLH1</i>	<ul style="list-style-type: none"> - Hereditary non-polyposis colorectal cancer (HNPCC). - Mismatch repair genes; mutations cause “microsatellite instability.”

<i>PMS2</i>	- Colonic polyps/cancer; also associated with gynecologic cancer.
<i>NF1</i>	- Neurofibromatosis type I; chromosome 17; AD. - Café au lait spots (hyperpigmented macules), axillary/groin freckling, neurofibromas (nerve sheath tumors presenting as nodules under the skin), weird CNS tumors (i.e., oligodendroglioma, ependymoma, meningioma), optic glioma (CN II tumor). - Classic disease that demonstrates variable expressivity , which means varying disease severity (I talk more about this stuff in my HY Genetics PDF).
<i>NF2</i>	- Neurofibromatosis type II; chromosome 22; AD. - Presents with acoustic schwannoma. Can be bilateral. - Meningioma.
<i>RB</i>	- Congenital retinoblastoma (i.e., leukocoria in 1-year-old) and osteosarcoma. - Tumor-suppressor gene; autosomal dominant (two hits required, but chance of second mutation is 100%, so AD not AR). - RB protein is normally in a complex with E2F, a transcription factor, repressing it and preventing cell cycle progression. CDK/Cyclin complexes then phosphorylate RB, releasing it from E2F. E2F then goes to the nucleus and transcribes genes → cell cycle progression. - NBME simply wants you to know that decreased RB phosphorylation is a wrong answer for what we'd expect in cancer cells.
<i>RET</i>	- Proto-oncogene → MEN 2A/2B. - Both MEN 2 syndromes have pheochromocytoma and medullary thyroid carcinoma. - MEN 2A has parathyroid adenoma or hyperplasia (same as MEN 1). - MEN 2B has Marfanoid body habitus and/or mucosal neuromas. - Same as with MEN 1, a HY point is that NBME Qs need not give all findings within a MEN syndrome. For instance, one NBME Q just gives medullary thyroid carcinoma alone, and the answer is <i>RET</i> . Another gives groin pain (urolithiasis due to hypercalcemia) + a neck tumor, and the answer is <i>RET</i> .
<i>TP53</i>	- Codes for p53 tumor-suppressor protein; halts the cell cycle in the setting of cellular damage so that DNA repair can occur. - Li-Fraumeni syndrome = congenital mutation in <i>TP53</i> leading to cancers of various organ systems. - HY answer on NBME for the gene mutated in cancer that has metastasized. - Pleiotropy = one gene has multiple effects; <i>TP53</i> is textbook example, since mutation can cause many unrelated cancers, such as pancreatic, ovarian, colon, etc.
<i>TSC1/2</i>	- Autosomal dominant; hamartin and tuberlin proteins. - Intellectual disability; periventricular nodules (tubers); adenoma sebaceum (aka angiofibromas, which are skin-colored/reddish papules on cheeks, nose, and in nasolabial folds); subungual fibromas (nailbed tumors); cardiac rhabdomyoma (ball-in-valve murmur that presents as diastolic rumble that attenuates with change of positioning); renal angiomyolipoma.
<i>VHL</i>	- Autosomal dominant; chromosome 3. - Renal cell carcinoma, PLUS retinal and/or cerebellar hemangioblastomas. - Pancreatic cysts can also be seen (on NBME). - The RCC need not be bilateral; don't confuse with angiomyolipoma of TSC. - New NBME Q shows picture of gross kidney lesion + tells you patient has cerebellar hemangioblastoma + retinal angioma; they ask what kind of kidney lesion they're showing → answer = "renal adenocarcinoma"; angioma is wrong answer.
<i>WT1</i>	- Can be isolated Wilms tumor; the answer on USMLE for kidney tumor in a kid almost always; presents as painless flank mass in 2-4-yr old. However Wilms tumor can also present as part of constellation syndromes: - Denys-Drash syndrome = gonadal agenesis + Wilms tumor. - WAGR syndrome = Wilms tumor, Aniridia, Genitourinary abnormalities, Retardation (can be associated with other genes as well, but just know that WT1 is associated). - Beckwith-Wiedemann syndrome = fetal macrosomia, macroglossia, hemihypertrophy, hypoglycemia, and Wilms tumor. Harder Q on 2CK form gives big baby with hemihypertrophy + doesn't mention Wilms tumor; they ask what else could be seen → answer = hypoglycemia.

Other HY Genes	
<i>ATP7B</i>	<ul style="list-style-type: none"> - Wilson disease; autosomal recessive; chromosome 13. - Copper overload. - Inability to secrete copper into bile from the liver. Copper is normally excreted by the body via secretion into bile. - ↑ urinary copper + ↓ serum ceruloplasmin (copper-binding protein in the blood; in the case of copper overload, body tries to minimize amount carried in blood). - Buzzy / pass-level detail is Keiser-Fleischer rings, which is copper deposited in the cornea of the eye. Vignette can give you what sounds like Wilson disease, and then the answer is “slit-lamp exam.” - Can cause ↑ LFTs with cirrhosis, hemolytic anemia, and Parkinsonism. - Copper deposits in basal ganglia, especially the putamen. - Parkinsonism in a young patient = Wilson until proven otherwise. - In old patient, Parkinsonism = Parkinson disease, normal pressure hydrocephalus, Lewy-body dementia, or progressive supranuclear palsy. - <u>Treat with the copper chelator penicillamine.</u>
<i>CFTR</i>	<ul style="list-style-type: none"> - Cystic fibrosis; chromosome 7; AR. - Codes for chloride channel. - Channel is normally located at cell surface; if mutated, it instead remains sequestered in the rough endoplasmic reticulum. - “Abnormal protein folding” is answer on NBME for result of <i>CFTR</i> mutations. - Delta F508 ($\Delta F508$) is most common mutation, which is deletion of phenylalanine 508. - CF is textbook example of allelic heterogeneity, which means many different mutations can cause the same disease. For this reason, most genotyping panels lack sensitivity, and sweat-chloride test showing >60 mEq/L is most diagnostic/accurate. A nasal test showing increased potential difference can also be performed. - Presents as child with chronic history of lung infections (<i>Pseudomonas</i> exceeds <i>S. aureus</i> after age 10). - Secretions in the alveoli and pancreatic ducts are inspissated (meaning desiccated / dried up within a lumen), making them sticky. This leads to exocrine pancreatic insufficiency, where enzymes can’t make it to the duodenum → fat-soluble vitamin malabsorption → NBME exams love vitamin E deficiency in CF in particular (presents as neuropathy). - Meconium ileus at birth; buzzy, but often not mentioned in questions. - Phenotypically normal siblings of affected children have 2/3 chance of being carrier (holds true for any AR disorder). - Ivacaftor/lumacaftor are newer treatments. They are known as potentiators/correctors, where the Cl^- channel structure, location, and function are improved.
<i>DMD</i>	<ul style="list-style-type: none"> - XR disorder caused by mutation in dystrophin. - Mutation results in disruption of α-/β-dystroglycan, which is required for proper internal cytoskeletal anchoring of the muscle cell to the extracellular matrix. - Presents with pseudohypertrophy, where muscles appear large but are replaced with fibroadipose tissue (connective tissue stromal cells). - Duchenne presents in a young boy who implements Gower maneuver to stand up (uses arms to walk up off the floor because leg muscles are weak). - Becker presents in adolescence or young adulthood (less severe form of Duchenne). - Duchenne is classically frameshift mutation; Becker is classically not frameshift.
<i>FBN1/2</i>	<ul style="list-style-type: none"> - Marfan syndrome; autosomal dominant; chromosome 15. - Codes for fibrillin, which is a glycoprotein that forms a sheath around elastin. - Tall, lanky body habitus with flat feet, chest wall abnormalities (i.e., pectus excavatum or carinatum), flat feet (pes planus), scoliosis, mitral valve prolapse (mid-systolic click), increased risk for aortic dissection (can retrograde propagate toward aortic root, causing root dilatation and aortic regurgitation [decrecendo diastolic murmur]). - Is not associated with berry/saccular aneurysms (unlike Ehlers-Danlos and ADPKD).
<i>FMR1</i>	<ul style="list-style-type: none"> - Fragile X; X-linked; caused by CGG trinucleotide repeat (TNR) expansion. - Results in hypermethylation of the gene and transcriptional silencing.


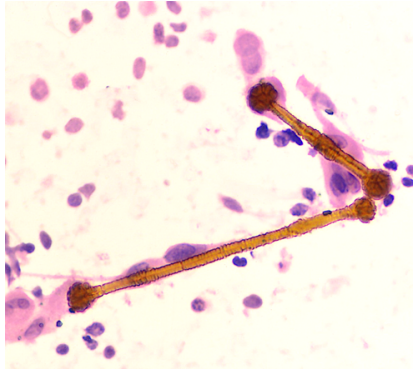
	<ul style="list-style-type: none"> - Presents as boy with large, everted ears; long, narrow jaw; macroorchidism; and intellectual disability. - Can sometimes be symptomatic in females if skewed X-inactivation (lyonization).
<i>FXN</i>	<ul style="list-style-type: none"> - Friedreich ataxia; Frataxin gene; GAA TNR expansion. - Presents with ataxia (you guessed it), scoliosis, cardiomyopathy, and decreased reflexes.
<i>G6PD</i>	<ul style="list-style-type: none"> - Glucose-6-phosphate dehydrogenase deficiency; X-linked recessive. - Presents as boy with hemolysis leading to jaundice (unconjugated hyperbilirubinemia) following oxidizing drug (e.g., sulfa, dapsone, primaquine). - Heinz bodies (denatured hemoglobin) and bite cells (degenerated RBCs due to removal of Heinz bodies) are seen.
<i>HFE</i>	<ul style="list-style-type: none"> - Hereditary hemochromatosis; autosomal recessive; chromosome 6. - Iron overload. - Mechanism USMLE wants is “increased intestinal iron absorption.” - Body has poor ability to excrete iron; occurs naturally via menses in women; otherwise there are minor losses via skin shedding. - Main iron regulation is via shutting off intestinal absorption; this is impaired in hemochromatosis. - Usually presents in adulthood in males first (because of menses in women). - Can present as “bronze diabetes” → hyperpigmentation due to hemosiderin deposition in skin + ↑ fasting sugars (iron deposition in tail of pancreas). - Miscellaneous other findings can be seen like infertility (iron deposition in hypothalamus, anterior pituitary, or gonads), cardiomyopathy, or arthritis (pseudogout). - Hereditary hemochromatosis, primary hyperparathyroidism, and hypothyroidism are 3 most important causes of pseudogout. I used to only discuss the former two with students over the years, but the latter shows up on a new 2CK NBME exam where they mention chondrocalcinosis (calcium deposition in cartilage). - USMLE wants you to know there is ↑ risk of hepatocellular carcinoma. There is easy NBME Q of hemochromatosis where they ask what patient is at increased risk for, and the answer is simply “hepatocellular carcinoma.” - Diagnose with ferritin >300 mg/dL. Transferrin saturation will also clearly be ↑. - It is exceedingly rare that ferritin is >300 in other conditions, however this can occur in lymphoma and leukemia, where ↑ ferritin is a poor prognostic marker in non-Hodgkin lymphoma. There is one NBME Q on 2CK where ferritin is 300 where it’s not hemochromatosis, but USMLE won’t play gotcha. - Treat with serial phlebotomy, not chelators. - Chelators such as deferoxamine or deferasirox are for secondary hemochromatosis due to transfusional siderosis (i.e., repeated blood transfusions that contain iron, for e.g., β-thalassemia major).
<i>HTT</i>	<ul style="list-style-type: none"> - Huntington disease; autosomal dominant; CAG TNR expansion on chromosome 4. - Presents as cognitive decline and choreoathetosis, usually in patient 30-40s. - Chorea = fast, purposeless, jerky movements. - Athetosis = slow, writing movements. - TNR disorders demonstrate anticipation, which means they become more severe and earlier-onset with each generation due to further expansion of the TNR, so the vignette can say the, e.g., 40-year-old patient had parent with similar symptoms appearing in his/her 50s. - If the USMLE asks you for which part of the brain is fucked up, choose caudate nucleus.
<i>NFKB1/2</i>	<ul style="list-style-type: none"> - Codes for NF-κB protein, which is involved in a myriad of cell-signaling processes. - For whatever magical reason, a repeated question across NBME exams wants you to know that “IκB releases NF-κB after undergoing phosphorylation.” - NF-κB is then free to go to the nucleus to upregulate transcription of 150+ genes. - Glucocorticoids (i.e., such as prednisone) partially exert their immunosuppressant effects by inhibiting NF-κB-mediated gene expression.
<i>PKD1/2</i>	<ul style="list-style-type: none"> - Autosomal dominant polycystic kidney disease. - The answer on USMLE if disease starts as an adult (i.e., 30s-40s). - Cysts are technically present early in life, but only become clinical as adult (i.e., ↑ BP and ↑ RFTs).

	<ul style="list-style-type: none"> - These patients have ↑ BP due to ↑ RAAS (compression of microvasculature of kidney due to enlarging cysts). - Can cause saccular (berry) aneurysms of the circle of Willis → risk for subarachnoid hemorrhage. - Highest yield point is that serial blood pressure checks are correct over circle of Willis MR angiogram screening. Latter is wrong answer on USMLE. MR angiogram screening of circle of Willis is only done when there is (+) family Hx of SAH or saccular aneurysms. - Cystic kidneys are part of "ciliopathies," which is obscure term that refers to conditions where cilia are abnormal. Polycystin is a protein required for cilia function on renal epithelium. - Most common extra-renal location for cysts is the liver (85% by age 30).
<i>PKHD1</i>	<ul style="list-style-type: none"> - Autosomal recessive polycystic kidney disease. - The answer on USMLE for cystic kidneys in pediatrics. - Can be associated with hepatic fibrosis.

Notable tumor markers	
AFP	<ul style="list-style-type: none"> - Alpha-fetoprotein. - Yolk sac tumor (aka endodermal sinus tumor) → the answer on USMLE for a testicular or ovarian tumor in a child. - Mixed germ cell tumors (if hCG also high).
ALP	<ul style="list-style-type: none"> - Alkaline phosphatase. - Placental ALP can sometimes be increased in seminoma. - Unrelated to increased ALP in bile duct obstruction or bone fractures.
CA 15-3	- Breast cancer.
CA 19-9	- Pancreatic cancer.
Calcitonin	<ul style="list-style-type: none"> - Increased in medullary thyroid carcinoma. - Normal role of calcitonin is to inhibit osteoclast activity.
CEA	<ul style="list-style-type: none"> - Carcinoembryonic antigen. - Colon cancer (although non-specific).
hCG	<ul style="list-style-type: none"> - Human chorionic gonadotropin. - Choriocarcinoma. - Mixed germ cell tumors (if AFP also high).
LDH	<ul style="list-style-type: none"> - Lactate dehydrogenase. - Dysgerminoma.
PSA	<ul style="list-style-type: none"> - Prostate-specific antigen. - Prostate cancer.

Hypersensitivity type relevant points	
Type	Mechanism
I	<ul style="list-style-type: none"> - Immediate (within minutes): Antigen binds to Fab region of IgE on mast cell; adjacent IgE crosslink; mast cell degranulates and secretes histamine + tryptase. - Late (within hours): Cytokines recruit inflammatory cells (e.g., eosinophils) → further inflammation. - HY examples are anaphylaxis (i.e., bee sting, peanut allergy), atopy / asthma.
II	<ul style="list-style-type: none"> - Antibody production against cells, tissues, receptors. - HY examples are Graves disease, Hashimoto thyroiditis, Goodpasture syndrome, pernicious anemia, HIT, ITP, rheumatic fever, myasthenia gravis, Lambert-Eaton, bullous pemphigoid, pemphigus vulgaris.
III	<ul style="list-style-type: none"> - Antibody-antigen complexes (i.e., antibodies simply bind to antigen and deposit; the antibodies do not target cells, tissues, or receptors). - HY examples are post-streptococcal glomerulonephritis, polyarteritis nodosa, SLE, arthus reaction, serum sickness.

IV	<ul style="list-style-type: none"> - T cell response (only HS type not associated with antibodies); can be mediated by either CD8+ or CD4+ T cells. - HY examples are PPD skin test for TB, contact dermatitis, graft-vs-host disease.
----	--

Notable Carcinogens	
Alcohol	- Oral/pharyngeal SCC; SCC of esophagus; hepatocellular carcinoma; breast cancer.
Aflatoxin	<ul style="list-style-type: none"> - Answer on USMLE if they mention peanut farming in China. - Can cause hepatocellular carcinoma.
Aniline dyes	<ul style="list-style-type: none"> - Answer on USMLE for hematuria in textile factory worker. - Can cause transitional cell carcinoma (TCC) of the bladder. - Aniline dyes are a type of industrial clothing dye.
Arsenic	<ul style="list-style-type: none"> - Answer on USMLE for Mees lines (white lines on nails), or palms + soles rash, in a gardener. - Arsenic is in many fertilizers; a small amount causes plants to flourish; poisoning seen in gardeners/landscapers, clearly.  <p>- A 2CK NBME Q gives pic of Mees lines in gardener → answer = arsenic.</p>
Asbestos	<ul style="list-style-type: none"> - Asbestosis → restrictive lung disease with ferruginous bodies and supradiaphragmatic / pleural plaques. Can develop into mesothelioma; NBME Q shows pic of ferruginous body and asks what cell initiates pulmonary fibrosis → answer = macrophage.  <p>(Ferruginous bodies in asbestosis)</p> <ul style="list-style-type: none"> - The pleural / supradiaphragmatic plaques can be described simply as “soft tissue densities” seen on CXR. - Mesothelioma → can appear as whitish cancer that circumferentially envelops the lungs; NBME Q asks for “mesothelial cells” as the answer. - Shipyard workers, construction workers, and electricians are buzzy professions on USMLE for asbestosis.
Benzene	- Leukemias.
Ethanol	<ul style="list-style-type: none"> - Highest yield = esophageal squamous cell carcinoma + hepatocellular carcinoma. - Breast cancer carries theoretical association but USMLE doesn't give a fuck.
Ionizing radiation	- Thyroid cancer; leukemias.

2-naphthylamine	- Main compound in some types of moth balls. - Collecting duct cancer (on NBME; I also discuss more in HY Renal PDF).
Nitrosamines	- Gastric cancer; associated with ↑ consumption of cured meats.
Processed meats	- Colorectal cancer.
Radon	- Adenocarcinoma of the lung in non-smokers. - Due to background radiation from the ground; considered the second-most important cause of lung cancer after smoking.
Smoking/tobacco	- Basically every cancer.
UV light	- Skin cancer.
Vinyl chloride	- Hepatic angiosarcoma.

Notable Paraneoplastic syndromes	
Gastric	- Acanthosis nigricans. Should be noted that almost always this finding simply means insulin resistance, but just be aware it can also be associated with visceral malignancies like gastric. “Visceral malignancy” is a general term that refers to main organ system cancers like the liver, pancreas, stomach, etc. - Sign of Leser-Trelat (sudden appearance of large numbers of seborrheic keratoses). Can occur with visceral malignancies, like gastric and pancreatic. - Virchow node (Troisier sign) is a palpable supraclavicular lymph node that is classically associated with gastric cancer, but can be visceral malignancy in general. There is also a 2CK NBME Q where Virchow node presents in a Hodgkin.
Ovarian	- Can cause dermatomyositis. Weird, but asked on an NBME question.
Pancreatic	- Migratory thrombophlebitis (Trousseau sign of malignancy).
Renal cell carcinoma	- Hypercalcemia (PTHrp secretion, same as squamous cell of lung). - Polycythemia (EPO secretion).
Lung cancer (general)	- Hypertrophic osteoarthropathy (clubbing + periostitis). - Periostitis is inflammation of the periosteum over the bone. - Classically associated with adenocarcinoma of the lung, but the USMLE doesn't specify. They'll just give you vignette of clubbing + hand pain, and the answer is “chest x-ray” for next best step in management.
Neuroblastoma	- Opsoclonus-myoclonus syndrome (dancing eyes).
Small cell carcinoma of the lung	- Cushing syndrome (ACTH secretion). - SIADH (ADH secretion). - Lambert-Eaton syndrome (Abs against presynaptic voltage-gated Ca^{2+} channels). - Cerebellar dysfunction/ataxia (anti-Hu/-Yo antibodies).
Squamous cell carcinoma of the lung	- Hypercalcemia/hypophosphatemia (PTHrp secretion). - PTHrp is not the same as endogenous PTH, which is suppressed due to negative-feedback from high calcium.
Thymoma	- Myasthenia gravis (Abs against postsynaptic nicotinic acetylcholine receptors). - Do CXR / chest CT in patients with MG. - Thymoma can also rarely cause pure-RBC aplasia (i.e., only RBCs are down).

Locations of metastases	
Metastasizes to	Cancer type
Spine/vertebrae	- Prostate, breast, and lung cancer all love to metastasize to spine/vertebrae. I've seen this across NBME Qs (and especially on 2CK Neuro CMS Qs), where they give neurologic findings in patients with cancer and want “epidural spinal cord metastases,” or “epidural spinal cord compression,” or “metastases to cauda equina” as answers. - There is a NBME Q where they give lytic lesions of the vertebrae in a vague 1-2-liner, where multiple myeloma isn't listed, and they just want “metastatic breast cancer” as the answer.

	- One of the highest yield general principles for USMLE is that prostate cancer causes osteoblastic metastases, which means they light up on a bone scan. Pretty much all other cancers cause osteolytic metastases. Occasionally some cancers such as breast can cause osteoblastic metastases, but for USMLE this application is essentially nonexistent; just remember prostate for this point.
Lung/brain	- Choriocarcinoma loves to go to lung and brain. If they give gynecologic question + mention pulmonary nodules or stroke-like presentation, this is HY for choriocarcinoma. Hydatidiform mole is a wrong answer here because, even though the latter can progress to invasive mole and choriocarcinoma, if the Q itself already mentions pulmonary or neuro findings, we know we already have the cancer, so choriocarcinoma is the better answer.
Ovaries	- Gastric cancer can metastasize hematogenously to ovaries. These are called Krukenberg tumors and will have signet ring cells on biopsy, which contain mucin.
Omentum	- USMLE loves direct extension to the omentum for ovarian cancer. There are two questions on the 2CK NBMEs where they say "omental thickening" and "omental caking."
Para-aortic lymph nodes	- Testicular and ovarian cancers. - I discuss specific lymph node drainages of cancers in my HY Immuno PDF, but this one is most important, so I'm including it here.

Malignancy-associated microbes	
<i>Aspergillus</i>	- Fungus that can produce aflatoxin, which increases risk of hepatocellular carcinoma.
<i>Clonorchis sinensis</i>	- Trematode (flake); a type of helminth (parasitic worm). - Can cause cholangiocarcinoma (cancer of the bile ducts). - Treat with praziquantel.
EBV	- Causes nasopharyngeal carcinoma and B-cell lymphomas (Hodgkin and NHL).
<i>Helicobacter pylori</i>	- Causes mucosa-associated lymphoid tissue (MALT) lymphoma, a type of B-cell lymphoma.
HepB/C	- Hepatocellular carcinoma.
HHV-8	- Kaposi sarcoma.
HIV	- Primary CNS lymphoma at CD4 counts generally <100/ μ L. - Immunodeficiency in general can increase risk of squamous cell carcinomas (e.g., anal SCC in MSM; esophageal SCC in smoking/alcohol; SCC of skin due to sunlight); NBME Qs can occasionally mention immunodeficiency in Qs to imply SCC.
HPV 16/18	- Squamous cell carcinoma (usually genital/anal).
HTLV	- Human T-cell lymphotropic virus. - Can cause cutaneous T-cell lymphoma (mycosis fungoides) and T-cell leukemia (Sezary syndrome).
<i>Schistosoma hematobium</i>	- Trematode. - Squamous cell carcinoma of the bladder (patient who swam in lake in Africa). - Don't confuse with transitional cell carcinoma of bladder, which is smoking, aniline (industrial) dyes, and 2-naphthylamine (moth balls).
<i>Strep bovis</i>	- Can increase risk of colorectal cancer (CRC), and endocarditis in setting of CRC.

IM Endocrine

Vasopressin conditions	
<ul style="list-style-type: none"> - Vasopressin (aka anti-diuretic hormone; ADH). - ADH is produced by both the supraoptic nucleus and paraventricular nucleus of the hypothalamus → stored in posterior pituitary. - ADH ↑ free water reabsorption by the medullary collecting duct (MCD) of the kidney by causing aquaporin insertion. - If ADH is ↑, we get ↑ free water reabsorption and dilution of our serum → serum sodium and osmolality ↓. Likewise, our urine becomes more concentrated, meaning urine osmolality and specific gravity ↑. - If ADH is ↓, we get ↓ free water reabsorption and concentration of our serum → serum sodium and osmolality ↑. Likewise, our urine becomes more dilute, meaning urine osmolality and specific gravity ↓. - The primary cells in the brain that recognize serum osmolality and contribute to the secretion of vasopressin are hypothalamic osmoreceptor cells. These are located in the organum vasculosum of the lamina terminalis (OVLT) and the subfornical organ, which detect changes in the osmolality of the blood. ↑ serum osmolality causes these osmoreceptors to stimulate the nearby supraoptic and paraventricular nuclei. 	
SIADH	<ul style="list-style-type: none"> - Syndrome of Inappropriate Anti-Diuretic Hormone secretion → means too much ADH (vasopressin secretion). - Central SIADH → follows head trauma, meningitis, brain cancer, and pain (latter on 2CK Surg). - Ectopic SIADH → small cell lung cancer secreting ADH. - Drug-induced ADH → ultra-rare on USMLE, but carbamazepine can do it. - Patient will have dilute serum and concentrated urine: <ul style="list-style-type: none"> - ↓ serum sodium, ↓ serum osmolality, ↓ serum specific gravity. - ↑ urinary osmolality, ↑ urinary specific gravity. - You must know serum sodium is normally 135-145 mEq/L. So in SIADH, it's <135. - Serum vs urinary osmolalities will be all over the place and you do <i>not</i> need to memorize values. They might say serum osmolality is 250 and urinary is 750, and then you say, "Well I can tell serum is dilute compared to urine, which sounds like SIADH." - Specific gravity will be 1.000-1.030 on USMLE. Sounds obscure, but it shows up quite a bit, particularly on 2CK Qs. It's to my observation that values 1.000-1.006ish are "dilute"; 1.024-1.030 are "concentrated." For 9/10 Qs, values will be what you expect. - As I talk about in detail in my HY Arrows PDF, only the medullary collecting duct osmolality will change in response to ADH. The USMLE will ask you for the osmolality of the urine at different nephron locations in comparison to serum, and the combo is: PCT isotonic; juxtaglomerular apparatus (JGA) hypotonic; MCD hypertonic. → The PCT is always isotonic no matter what; the JGA (at top of thick ascending limb of loop of Henle) is always hypotonic no matter what; the MCD is clearly hypertonic in SIADH since we're pulling free water out of the urine. - "Fluid restriction" is first answer in diagnosis on 2CK. We want to see how serum/urinary values change in response. - Demeclocycline is answer on 2CK offline NBME 8 for treatment of SIADH. Demeclocycline is technically a tetracycline antibiotic but isn't used because it can cause insensitivity to ADH at the kidney (i.e., nephrogenic diabetes insipidus). So we essentially cause a 2nd problem that cancels out the 1st problem. - Conivaptan and tolvaptan are ADH receptor antagonists that can be used for SIADH.
DI	<ul style="list-style-type: none"> - Central diabetes insipidus → means not enough ADH secretion by hypothalamus, or the posterior pituitary is unable to release it properly. - Nephrogenic DI → insensitivity to ADH at the kidney (serum ADH is ↑). - Similar to central SIADH, central DI can be caused by head trauma, meningitis, and cancer.

	<ul style="list-style-type: none"> - Nephrogenic DI is caused by lithium, demeclocycline, hypercalcemia, and NSAIDs. - There is an NBME Q that asks about a patient's response to ADH who is on chronic NSAIDs, and the answer is "\leftrightarrow Response to ADH" and "\leftrightarrow urinary osmolality" (meaning no change). - 2CK Q gives patient with primary hyperparathyroidism and $\uparrow\uparrow$ serum calcium + nephrogenic DI; Q asks cause of the DI \rightarrow answer = hypercalcemia. High calcium can cause renal insensitivity to vasopressin. - Serum vs urinary values are the opposite of SIADH: <ul style="list-style-type: none"> - \uparrow serum sodium (>145 mEq/L), \uparrow serum osmolality, \uparrow serum specific gravity. - \downarrow urinary osmolality, \downarrow urinary specific gravity. - PCT isotonic; JGA hypotonic; MCD hypotonic. \rightarrow The PCT is always isotonic no matter what; the JGA is always hypotonic no matter what; the MCD is clearly hypotonic in DI since we're not pulling free water out of the urine. - When we are trying to first diagnose DI, the first thing we do is fluid restriction, same as with SIADH. We want to see how serum/urinary values change first. - After we determine that the urine is staying dilute + the serum is staying concentrated, the next best step is desmopressin (analogue of vasopressin). If the urine gets more concentrated, (i.e., if the drug works), we know central DI is the diagnosis and we're merely deficient in ADH. - If desmopressin doesn't work, we know we have nephrogenic DI. I should point out that even in nephrogenic DI, desmopressin might work <i>but only very little</i>, whereas with central DI, administration will $\uparrow\uparrow$ urinary osmolality robustly. It will be obvious on USMLE. But my point is, don't say, "Oh well desmopressin worked like 5% so we can't have nephrogenic DI here." - Treatment for central DI is therefore desmopressin. - Treatment for nephrogenic DI is NSAID + a thiazide. Sounds weird, but \downarrow Na^+ reabsorption induced by thiazides in the early-DCT promote compensatory \uparrow Na^+ reabsorption in the PCT, where water follows Na^+ and our net loss of fluid is less than without the thiazide. In healthy individuals, however, they <i>will</i> lose more net fluid with the thiazide. The NSAID presumably \downarrow renal blood flow, which will \downarrow GFR and \downarrow net fluid loss. - There is difficult 2CK NBME Q where they say patient is on lithium + has \uparrow urinary output, and fluid restriction is wrong answer to this question (I say hard because 9/10 times, fluid restriction is correct when it's listed); answer = NSAID + thiazide diuretic. The implication is, if it's obvious what the patient's diagnosis is already nephrogenic DI, going straight to Tx is acceptable.
PP	<ul style="list-style-type: none"> - Psychogenic polydipsia means the patient is simply drinking too much. - Both the urine and serum will be dilute. - Serum vs urinary values are the opposite of SIADH: <ul style="list-style-type: none"> - \downarrow serum sodium (<135 mEq/L), \downarrow serum osmolality, \downarrow serum specific gravity. - \downarrow urinary osmolality, \downarrow urinary specific gravity. - I'd say 3/4 Qs on USMLE are obvious and will say some psych patient is drinking lots to "clear himself from evil spirits," etc. - Probably 1/4 Qs won't be an obvious psych vignette, but will just show you the lab values where you have to say, "The urine and serum are <i>both</i> dilute, so this is psychogenic polydipsia." - First step in diagnosis is fluid restriction in order to see how urinary/serum values change.

Acromegaly

- Caused by excess growth hormone secretion (usually by a tumor) following closure of the growth plates (\uparrow GH secretion prior to growth plate closure causes gigantism).
- As mentioned earlier, GH goes to the liver, which causes it to secrete IGF-1. It is then IGF-1 that induces growth effects at tissues. An NBME Q gives easy vignette of acromegaly and then asks what you check; serum GH is wrong; answer is serum IGF-1.

- Acromegaly causes prognathism (lantern jaw), large ears/nose, arthritis and carpal tunnel syndrome (due to ↑ joint and tendon growth), enlargement of hands/feet, hypertension, type II diabetes (GH causes insulin resistance), and ↑ risk of arrhythmia and cardiomyopathy.

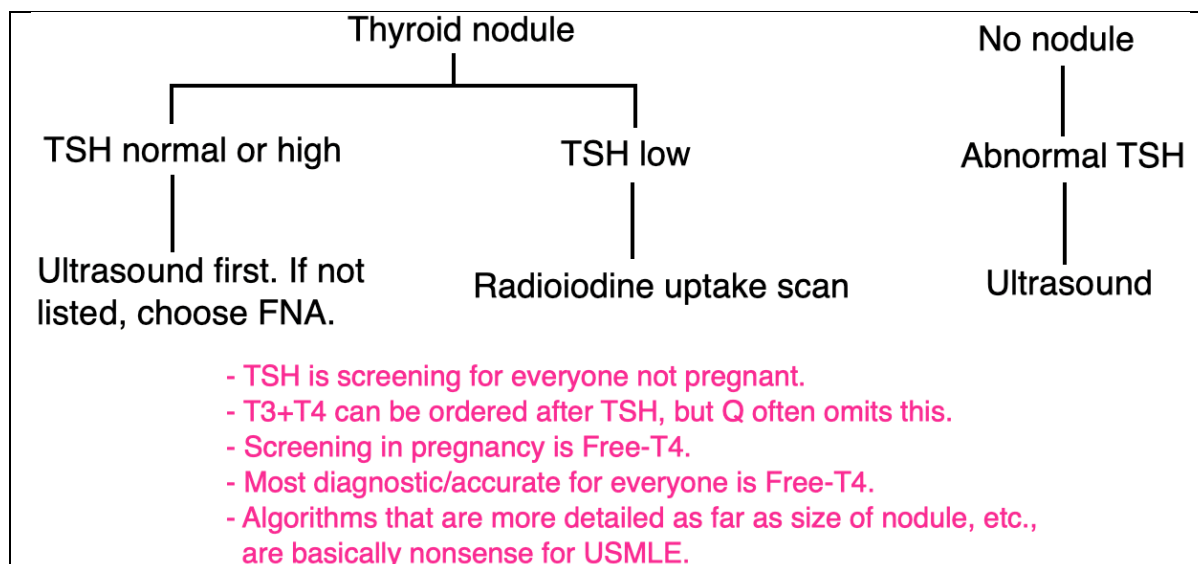
- Treatment is somatostatin analogue (octreotide). Somatostatin is aka growth hormone-inhibiting hormone (GHIH) and shuts off its secretion from the anterior pituitary. It also ↓ secretion of insulin and glucagon from the pancreas.

HY Thyroid diagnoses	
Hashimoto thyroiditis	<ul style="list-style-type: none"> - Autoimmune destruction of thyroid gland. - Lymphocytic infiltrate seen on biopsy (asked on NBME). - Anti-microsomal (aka anti-thyroperoxidase) + anti-thyroglobulin antibodies. - ↓ T₃, ↓ T₄, ↑ TSH. - ¹³¹I uptake scan is ↓ or patchy (i.e., the gland is not producing hormone). - Buzzy findings are weight gain, brittle hair, dry/doughy skin, and cold intolerance. The USMLE often will omit these findings because they're too easy. - HY additional findings I've seen show up in NBME Qs are: bradycardia (55-60), menstrual irregularity, dysthymia/depression/apathy, carpal tunnel syndrome (due to glycosaminoglycan [GAG] deposition), ↑ cholesterol, proximal muscle weakness with ↑ creatine kinase (hypothyroid myopathy); transaminitis (sounds weird, but LFTs can be ↑). - Associated with other autoimmune diseases (e.g., type I diabetes, pernicious anemia, vitiligo) and immunodeficiencies (e.g., IgA deficiency). For USMLE, a HY big-picture concept is that "Autoimmune diseases go together," where if you have one autoimmune disease, there's ↑ risk of other autoimmune diseases. The strict HLA associations aren't important (outside of HLA-B27). In addition, "Autoimmune diseases and immunodeficiencies go together," where having autoimmune disease in general ↑ risk of immunodeficiencies, and vice versa. - ↑ risk of non-Hodgkin lymphoma (e.g., primary CNS lymphoma). - Tx = levothyroxine or triiodothyronine.
Graves disease	<ul style="list-style-type: none"> - Activating autoantibody against TSH receptor. This antibody is called thyroid-stimulating immunoglobulin (TSI). - ↑ T₃, ↑ T₄, ↓ TSH. - Lymphocytic infiltrate + hyperplastic thyroid follicles seen on biopsy. - ¹³¹I uptake scan shows diffusely ↑ uptake. - Exophthalmos (aka proptosis; protrusion of eyes) and pretibial myxedema (non-pitting edema of shins due to GAG deposition) are specific findings in Graves. The vignette need not mention either of these findings, but if the Q specifically tells you "there's no exophthalmos," they're saying it's not Graves. - Buzzy findings are tachycardia, heat intolerance, sweating, and palpitations. - Myopathy can also occur with ↑ CK, but USMLE tends to give this finding in hypothyroidism. - Can cause atrial fibrillation in younger patients (normally AF is elderly). - "Thyroid storm" is an acute exacerbation of Graves, often precipitated by a stress factor such as surgery, trauma, or infection, where thyroid hormone production goes ↑↑↑, causing dangerous physiologic responses, such as hyperthermia, tachycardia, and altered mental status. - Thyroid storm can also cause adrenal crisis (i.e., acute ↓ in blood pressure due to rapid consumption of cortisol), especially in those with concurrent adrenal insufficiency taking exogenous steroids. Tx for the low BP is IV glucocorticoid (i.e., hydrocortisone or methylprednisolone). - Tx for general Graves is thionamides (propylthiouracil [PTU] and methimazole).

	<ul style="list-style-type: none"> - PTU and methimazole both inhibit thyroperoxidase; PTU has an additional MOA of inhibiting 5-deiodonase. - Both PTU and methimazole can cause neutropenia/agranulocytosis. - Propranolol is used for tachycardia in hyperthyroidism (beta-blockade inhibits 5-deiodonase). - Oral prednisone is specifically used for Tx of exophthalmos, not thionamides. - Tx of thyroid storm on USMLE is tetrad of: 1) PTU, 2) propranolol, 3) steroids, and 4) potassium iodide (shuts off thyroid gland due to Wolff-Chaikoff effect). - Wolff-Chaikoff effect is a transient ↓ in thyroid hormone synthesis in the setting of acute ↑ in iodide exposure, which prevents excessive thyroid hormone production. Tangentially, if a USMLE Q gives you a patient exposed to radioactive iodine (e.g., working in a laboratory), the Tx is potassium iodide, which saturates the thyroid gland with “regular” iodide and prevents uptake of the radioiodine, thereby preventing destruction of the gland.
deQuervain thyroiditis	<ul style="list-style-type: none"> - Aka subacute granulomatous thyroiditis, or just simply subacute thyroiditis. - Mechanism is viral infection followed by a painful/tender thyroid. There is inflammation of the thyroid gland, which causes the spacing between the cells to increase slightly, allowing for the release of pre-formed thyroid hormone into the blood. Therefore we have ↓ TSH, ↑ T3, ↑ T4, ↓ ¹³¹I uptake. - The gland is not over-producing thyroid hormone. This is why uptake is not increased. - Subacute granulomatous thyroiditis can be either hypo- or hyperthyroid. The key detail you need to know is that uptake is always decreased even if the patient is hyper-. - DeQuervain vignettes will almost always be given as hyperthyroidism because the USMLE wants to specifically assess that you know uptake is decreased. If they give you hypo-, of course you’ll select decreased for uptake. - Decreased uptake applies to all thyroiditis conditions (i.e, deQuervain, drug-induced, and postpartum). - Viral infections are often asymptomatic, so most deQuervain vignettes will not mention the viral infection.
Drug-induced thyroiditis	<ul style="list-style-type: none"> - Caused by lithium or amiodarone on USMLE. - Can in theory be hypo-, eu-, or hyperthyroid. - Will usually present on USMLE as painless hypothyroidism in patient being treated for bipolar disorder (lithium) or started on new anti-arrhythmic (amiodarone). - Will present with ↓ ¹³¹I uptake, where inflammation of the gland can sometimes cause leakage of thyroid hormone into the blood, but the gland itself is not demonstrating increased production of hormone.
Subclinical hypothyroidism	<ul style="list-style-type: none"> - ↑ TSH, ↔ T3, ↔ T4. - In subclinical hypothyroidism, the patient will be asymptomatic (hence subclinical) and will have normal T3 and T4, despite an elevated TSH. - Most patients with subclinical do not need to be treated. - Don’t treat unless TSH >10, patient is pregger, or anti-Hashimoto Abs are +.
Euthyroid sick syndrome	<ul style="list-style-type: none"> - Vignette will give patient being weaned from a ventilator, or someone who’s had recent major trauma or surgery. - ↔ TSH, ↔ T4, ↓ T3, ↑ rT3. - Etiologies are manifold, but one proposed mechanism is that in times of stress (usually acute), spikes in cortisol and other inflammatory mediators can inhibit peripheral conversion of T4 to T3. This causes T3 to go down. - T4, however, rather than being detectable in excess, is converted to an inactive form of thyroid hormone called reverse T3 (rT3), so rT3 is high. - T4 is therefore still in the normal range, as is TSH (presumably because T4 is normal).

	<ul style="list-style-type: none"> - Call it weird all you want, but USMLE asks this. This is one of the most “underrated” thyroid diagnoses, as students will often have heard of it but then disregard it, thinking it’s minutiae and probably won’t show up.
Toxic adenoma	<ul style="list-style-type: none"> - Autonomously secreting thyroid nodule (aka hot nodule). - ^{131}I scan shows uptake onto into the area of a single nodule. - $\uparrow \text{T}_3$, $\uparrow \text{T}_4$, $\downarrow \text{TSH}$. - Not malignant (i.e., no metastatic potential).
Toxic multinodular goiter	<ul style="list-style-type: none"> - Autonomously secreting thyroid nodules (i.e., many hot nodules). - ^{131}I scan shows multinodular uptake. - $\uparrow \text{T}_3$, $\uparrow \text{T}_4$, $\downarrow \text{TSH}$. - Not malignant (i.e., no metastatic potential). - I don’t think I’ve ever seen this as a correct answer on USMLE, but it shows up quite a bit as a distractor, e.g., for deQuervain Qs. - Occurs in elderly. You might get a younger patient with hyperthyroidism due to deQuervain, and you can eliminate toxic multinodular goiter because 1) the patient is young, and 2) deQuervain is painful/tender, whereas TMG is not.
Factitious thyrotoxicosis	<ul style="list-style-type: none"> - Aka surreptitious thyrotoxicosis. - USMLE need not mention the patient is a pharmacist (implying access to the hormone). - Q will give hyperthyroid patient with small, non-palpable thyroid gland (atrophic due to suppressed TSH). - As mentioned earlier, T_4 is converted to T_3, but T_3 isn’t converted to T_4. - So if thyroxine is administered, we will have $\uparrow \text{T}_3$, $\uparrow \text{T}_4$, $\downarrow \text{TSH}$. - If triiodothyronine is administered, we will have $\uparrow \text{T}_3$, $\downarrow \text{T}_4$, $\downarrow \text{TSH}$.

Thyroid nodule evaluation
<ul style="list-style-type: none"> - When evaluating for thyroid cancer, the first step is “palpation of thyroid gland” before “check serum TSH.” There is an NBME Q for 2CK where both are listed and palpation is correct (i.e., do a history and exam before jumping into tests). - Once a nodule is palpated, <i>then</i> serum TSH is the next best step. - If patient with nodule has normal or high TSH (i.e., is euthyroid or hypothyroid), do ultrasound before fine-needle aspiration (FNA). This is assessed on the new 2CK Free 120, where ultrasound is correct over FNA for evaluation of thyroid nodule. It had long been pushed in resources that ultrasound is always wrong. But this is on Free 120. - 2CK IM CMS Q gives euthyroid patient with nodule where FNA is the answer, but ultrasound isn’t listed. - So my conclusion (based on NBME/Free 120 content; not my opinion) is: for eu- or hypothyroid patient with thyroid nodule, ultrasound is correct over FNA if both are listed. If ultrasound isn’t listed, choose FNA. - If patient has low TSH (i.e., is hyperthyroid), do ^{131}I uptake scan, not ultrasound. - Since carcinomas are non-secretory of thyroid hormone, if a patient is hyperthyroid, we’re not concerned about carcinoma, which is why we don’t go the ultrasound then FNA route. We just do uptake to better see if the patient’s etiology for hyperthyroidism is Graves (diffuse), toxic adenoma (single nodular uptake), or toxic multinodular goiter (multifocal nodular uptake). - A caveat about the above algorithm for nodule evaluation is that if a patient has hyperthyroidism (i.e., low TSH) <i>and does not have a nodule</i>, then you will choose ultrasound over uptake scan. I know this sounds annoying, but USMLE assesses this. There is a new NBME Q where they give low TSH in young patient with no mention of nodule, and the answer is ultrasound over uptake scan. But in Qs where TSH is low and the patient has a nodule, the answer is uptake scan first over ultrasound. If you want a high score, then know the difference.



Thyroid in pregnancy

- For pregnancy on USMLE, choose the combo of **no change TSH, no change free T4, ↑ total T4** for women who have no thyroid symptoms.
- **Estrogen** causes ↑ thyroid-binding globulin (TBG) production by the liver. TBG is the protein carrier molecule for thyroid hormone in the blood. An NBME Q asks for which hormone causes the ↑ TBG in pregnancy → answer = estrogen, not progesterone.
- Free T4 is the physiologically active form of thyroid hormone. T4 protein-bound to TBG (99%) has minimal effect. Free T4 + TBG-bound T4 = total T4.
- TBG will mop up free T4, causing free T4 to transiently decrease and TSH to rise (less negative feedback). This rise in TSH will stimulate more production of T4 by the thyroid gland, making total T4 go up. The absolute amount of free T4 will increase back to normal, thereby suppressing TSH back to normal. But the total amount of T4 is now increased – i.e., free T4 is normal again, but TBG-bound T4 is higher.
- T3 is normal because free T4 is normal. Free T4 is peripherally converted to T3. I've never seen anything about "free T3" on NBME material and I wouldn't worry about it.
- A student might say, "Wait, but why are you giving the above bold arrows if you just gave me all sorts of transient changes in the arrows based on TBG?." It's because the bold arrows are what the USMLE wants. Pregnant women who are euthyroid will have normal free T4 and increased total T4, and their TSH will be normal. The changes due to TBG rising are likely synchronous and slow enough that the patient's TSH and free T4 stay within reference ranges.
- Postpartum (silent) thyroiditis can result in either hypo- or hyperthyroidism following parturition. These arrows are unrelated to the aforementioned ones. The highest yield point you need to know is that ¹³¹I uptake into the thyroid gland is low, even if the patient is hyperthyroid. This is the same for deQuervain and drug-induced thyroiditis, where uptake is always low. This is because with thyroiditis conditions, there is merely increased spacing between the cells of the thyroid gland due to inflammation, allowing thyroid hormone to leak out into the blood. The gland itself is not excessively producing thyroid hormone. Then we have negative feedback causing low TSH, and in turn less stimulation of the thyroid gland, which is why uptake is low.
- If USMLE asks you about levothyroxine dosing during pregnancy, the answer is "increase dose by 50%."
- Avoid methimazole in first trimester (teratogenic).
- PTU is the answer for thyroid storm during pregnancy, even though longer-term use in 2nd and 3rd trimesters isn't considered ideal because of hepatic toxicity risk.

Thyroid in pediatrics	
Thyroglossal duct cyst	<ul style="list-style-type: none"> - Benign, painless, midline neck mass in a school-age kid that arises from a persistent thyroglossal duct (i.e., the embryologic remnant of the thyroid gland's descent from the base of the tongue to its final position in the neck). - 2/3 of Qs will give a painless midline neck lump that moves upwards with swallowing or protrusion of the tongue (due to its attachment to the hyoid bone and/or the base of the tongue). - 1/3 of Qs won't mention the buzzy upward movement with swallowing or protrusion of the tongue; instead, it will just say a kid has a painless midline neck mass just inferior to the hyoid bone that demonstrates ^{99}Tc uptake.
Lingual thyroid	<ul style="list-style-type: none"> - Obscure cause of hypothyroidism that shows up on an offline NBME. - Refers to presence of ectopic thyroid tissue located at the base of the tongue due to failure of the thyroid gland to descend from the foramen cecum. - This ectopic tissue may be the only functioning thyroid tissue in the body, resulting in hypothyroidism. - The USMLE Q will say a kid has hypothyroidism + a midline neck lump located high in the neck. They say nothing about protrusion of the tongue or uptake into the mass. - Can sometimes cause dysphagia (trouble swallowing), dysphonia (voice changes), or dyspnea (difficulty breathing).
Cretinism	<ul style="list-style-type: none"> - Aka congenital hypothyroidism. - Most common causes are iodine deficiency in the mother during pregnancy (worldwide) and fetal thyroid dysgenesis (western countries). - Leads to mental retardation (poor myelin sheath development), impaired bone growth, hypotonia, macroglossia, and protuberant abdomen (due to umbilical hernia; can be confused with kwashiorkor, which is protein-calorie malnutrition causing ascites). - Screened for at birth using the heel-prick test to prevent exacerbation.
TBG deficiency	<ul style="list-style-type: none"> - The USMLE does not expect you to know about some obscure condition called thyroid-binding globulin deficiency. The reason they ask about this is because the role of TBG on thyroid hormones in pregnancy is exceedingly high-yield, so if you know the reasoning/mechanism behind the latter, you can easily infer what would be seen in TBG deficiency (i.e., the inverse). - \leftrightarrow TSH, \leftrightarrow T3, \leftrightarrow free T4, \downarrow total T4. - In pregnancy, since TBG is high, this ultimately results in high total T4 despite a normal free T4. So the student can easily infer, "Well, if our TBG merely is low, rather than high, then total T4 must be low while free is same. Sort of like pregnancy but just the opposite direction."

Parathyroid points
<ul style="list-style-type: none"> - Parathyroid hormone (PTH) functions to \uparrow serum Ca^{2+} and \downarrow serum PO_4^{3-}. - Parathyroid hormone (PTH) functions to increase serum calcium in three main ways: <ul style="list-style-type: none"> 1) Pulls calcium out of the bone and puts it in the blood. <ul style="list-style-type: none"> o PTH binds to osteoblasts, which will then express RANK-L on their cell surface, which will bind to RANK receptor on the surface of osteoclasts. Osteoclasts then resorb (break down) bone. The calcium enters the blood, increasing serum calcium. 2) Increases renal reabsorption of calcium. <ul style="list-style-type: none"> o PTH causes Ca^{2+} reabsorption at the late-DCT of the kidney by increasing expression of an apical calcium channel. 3) Upregulates 1α-hydroxylase. <ul style="list-style-type: none"> o PTH upregulates 1α-hydroxylase in the PCT of the kidney, which converts inactive 25-OH-vitamin D3 (calcidiol) into active 1,25-(OH)$_2$-D3 (calcitriol). o 1,25-(OH)$_2$-D3 then goes to the small bowel, where it increases absorption of both calcium and phosphate.

- PTH decreases serum phosphate by inhibiting its reabsorption in the PCT of the kidney.
 - o PTH causes the downregulation of apical PCT phosphate transporters.
 - o If PTH is low, we don't get downregulation of these transporters, too much phosphate is reabsorbed, and serum PO_4^{3-} goes up.

Vitamin D pathologies for IM	
Rickets/Osteomalacia	<ul style="list-style-type: none"> - Rickets = vitamin D deficiency in children. - Osteomalacia = vitamin D deficiency in adults. - Calcium and phosphate are both low because vitamin D is needed for intestinal absorption of both. - PTH goes up because calcium is low (decreased negative feedback). - It should be noted that in vitamin D deficiency caused by renal failure, phosphate is high, not low, because the effect of the renal failure on phosphate levels wins over the mere vitamin D deficiency. In renal failure, the kidney cannot downregulate the PCT phosphate reabsorption channels, thereby increasing absorption. - Renal failure always has high phosphate, even though Vit D3 activation is low. - Renal failure + low vitamin D: <ul style="list-style-type: none"> o \downarrow serum Ca^{2+}, \uparrow serum PO_4^{3-}, \uparrow PTH. - No renal failure + low vitamin D (i.e., rickets/osteomalacia): <ul style="list-style-type: none"> o \downarrow serum Ca^{2+}, \downarrow serum PO_4^{3-}, \uparrow PTH.
Renal failure	<ul style="list-style-type: none"> - Inability for PTH to activate 1α-hydroxylase in the PCT of the kidney. - \downarrow 1,25-D3 synthesis, but 25-D3 is normal. - 25-D3 doesn't build up physiologically. If there is "extra" 25-D3 because it is not being converted to 1,25-D3, then it gets shunted sideways to another inactive form called 24,25-D3 (asked on NBME). - Osteomalacia resulting from renal failure is called renal osteodystrophy.

Hyperparathyroidism conditions	
Primary	<ul style="list-style-type: none"> - \uparrow Ca^{2+}, \downarrow PO_4^{3-}, \uparrow PTH. - Primary hyperparathyroidism is usually due to a PTH-secreting adenoma, but can also be due to diffuse four-gland hyperplasia. - Can be part of MEN-1 or -2A (discussed later). - \uparrow Urinary Ca^{2+}, \uparrow serum Ca^{2+}, \uparrow urinary cAMP. - Some students will immediately think there's an erratum with the above arrows. There's not. Relax. - In primary hyperparathyroidism, PTH will be high. PTH functions to reabsorb calcium in the late-DCT of the kidney, so in theory, you'd think urinary calcium would be low, not high. Sounds logical. - However, even though more Ca^{2+} is indeed reabsorbed in the late-DCT, since serum Ca^{2+} is high in primary hyperparathyroidism, <i>more calcium is filtered through the glomerulus to begin with</i>. So even though more is reabsorbed distally, the urinary calcium <i>is still high</i> because we had more to start with. - PTH causes increased urinary cAMP. This is a weird variable that you should be aware of. PTH acts through G-α-s G-proteins, where adenylyl cyclase activity and, in turn, cAMP are increased.
Secondary	<ul style="list-style-type: none"> - \downarrow Ca^{2+}, \uparrow PO_4^{3-}, \uparrow PTH, \downarrow 1,25-D3. - Secondary hyperparathyroidism is due to renal failure. - There are two reasons why calcium is low: <ol style="list-style-type: none"> 1) The kidney cannot reabsorb it in the late-DCT like it's supposed to.

	<p>2) The kidney cannot synthesize activated 1,25-D3 in the PCT like it's supposed to. Since 1,25-D3 absorbs calcium in the small bowel, and 1,25-D3 levels are lower, serum calcium will also be lower.</p> <ul style="list-style-type: none"> - The low serum calcium will cause PTH to go up (decreased negative-feedback at the calcium-sensing receptors on the parathyroid glands). - Since the etiology for the increased PTH secretion is not the parathyroid glands themselves, we call this secondary hyperparathyroidism. If the etiology is due to the parathyroid glands themselves (i.e., adenoma or diffuse hyperplasia), we call that primary hyperparathyroidism. - The calcium and phosphate arrows for secondary hyperPTH are the opposite of primary hyperPTH. - Phosphate is high in renal failure, despite the high PTH, because the kidney is not able to downregulate the PCT phosphate transporters, so there is too much phosphate reabsorption.
Tertiary	<ul style="list-style-type: none"> - $\uparrow \text{Ca}^{2+}$, $\uparrow \text{PO}_4^{3-}$, $\uparrow \text{PTH}$. - In order to understand tertiary hyperparathyroidism, let's first review secondary hyperparathyroidism: - Patients with renal failure will initially develop secondary hyperparathyroidism, where calcium is low, phosphate is high, and PTH is high. Calcium is low due to failure of reabsorption at the late-DCT of the kidney and because of decreased synthesis of activated vitamin D3 (leading to decreased small bowel absorption). Phosphate is high due to failure to downregulate PCT reabsorption pumps (i.e., more pumps reabsorb phosphate). PTH is high because calcium is low (less negative feedback). - Tertiary hyperparathyroidism results from hyperplasia of the parathyroid glands in patients with long-standing secondary hyperparathyroidism, such that even if the renal failure is brought under control and serum calcium is brought back into the normal range, PTH continues being autonomously secreted at higher basal levels than prior to the renal disease, effectively resetting the body's setpoint for calcium homeostasis. - This causes a rise in serum calcium in a patient with renal failure. This should immediately raise a red flag for tertiary hyperPTH, since renal failure patients will almost always have low, not high, calcium. - Even though the parathyroid glands will be hyper-secreting PTH, this is not primary hyperparathyroidism, since the etiology for the high PTH was not idiopathic adenoma or hyperplasia. - Phosphate is high, not low, because the patient has renal failure. Phosphate is always high in renal failure. Even though PTH is high, remember that the kidney can't downregulate the PCT reabsorption pumps the way they're supposed to.

Hypoparathyroidism conditions	
DiGeorge	<ul style="list-style-type: none"> - $\downarrow \text{Ca}^{2+}$, $\uparrow \text{PO}_4^{3-}$, $\downarrow \text{PTH}$, \downarrow T cell levels, \leftrightarrow B cell levels. - Mechanism is most frequently 22q11 deletion, resulting in agenesis of the 3rd and 4th pharyngeal pouches. - The 3rd pouch becomes the thymus + two inferior parathyroids. - The 4th pouch becomes the two superior parathyroids. - Tetralogy of Fallot and truncus arteriosus are common heart defects. - Agenesis of the parathyroid glands \rightarrow primary hypoparathyroidism \rightarrow low calcium + high phosphate. - DiGeorge is characterized by T cell deficiency. Recurrent viral, fungal, and protozoal infections are characteristic. - Absent thymic shadow = T cell deficiency \rightarrow DiGeorge. - Scanty lymph nodes/tonsils = B cell deficiency \rightarrow Bruton agammaglobulinemia. - If Q says kid has both absent thymic shadow <i>and</i> scanty lymph nodes/tonsils \rightarrow answer = SCID.
Post-thyroidectomy	- $\downarrow \text{Ca}^{2+}$, $\uparrow \text{PO}_4^{3-}$, $\downarrow \text{PTH}$.

	<ul style="list-style-type: none"> - Thyroidectomy can result in removal of or damage to the parathyroid glands, resulting in decreased PTH secretion and, in turn, hypocalcemia. Phosphate goes up because there is increased renal reabsorption (PTH normally downregulates apical PCT phosphate transporters, thereby promoting excretion). - Twitching of the masseter with stimulation is called Chvostek sign of hypocalcemia. - Hypocalcemia causes “up” findings – i.e., muscle tetany and hyperreflexia. - Trousseau sign of hypocalcemia is carpopedal spasm with blood pressure cuff inflation (i.e., twitching of the hand/wrist). The USMLE can give you either Chvostek or Trousseau sign when Ca^{2+} is low. - Hypercalcemia, in contrast, causes “down” findings – i.e., muscle flaccidity and hyporeflexia. - Do not confuse Trousseau sign of hypocalcemia with Trousseau and Troisier signs of malignancy. - Troisier sign of malignancy is a palpable left supraclavicular lymph node sometimes seen in visceral malignancy (aka Virchow node). - Trousseau sign of malignancy is migratory thrombophlebitis classically seen in head of pancreas adenocarcinoma (but can be other adenocarcinomas, such as bronchogenic).
Hypomagnesemia	<ul style="list-style-type: none"> - $\downarrow \text{Ca}^{2+}$, $\uparrow \text{PO}_4^{3-}$, $\downarrow \text{PTH}$, $\downarrow \text{Mg}^{2+}$. - Alcoholics are susceptible to hypomagnesemia as a result of dietary deficiency (EtOH is 7kcal/g, so they fill up on alcohol). - Low magnesium can cause hypocalcemia and hypokalemia nonresponsive to supplementation (i.e., you give calcium or potassium for low serum levels, but the serum levels do not appreciably rise). - Basal levels of magnesium are required for proper functioning of the parathyroid gland, so low magnesium can cause low PTH secretion. - Patients with hypomagnesemia may indeed have completely normal serum levels for calcium, phosphate, and PTH, but if we are forced to choose arrows, we would choose a $\text{Ca}^{2+}/\text{PO}_4^{3-}/\text{PTH}$ combo that reflects low PTH secretion. - The Step 2 exam will often just say an alcoholic has low calcium or potassium nonresponsive to supplementation, and then the next best step in management is “check serum magnesium levels.” This isn’t hard at all. But some students will be like “Oh wow.”

Other calcium derangement conditions	
Paraneoplastic PTHrp	<ul style="list-style-type: none"> - Squamous cell carcinoma of the lung and renal cell carcinoma both secrete parathyroid hormone-related peptide (PTHrp). <i>This is not the same as endogenous PTH.</i> - USMLE Qs for renal cell carcinoma and squamous cell of the lung will have: <ul style="list-style-type: none"> o \uparrow Serum Ca^{2+}, \downarrow serum PO_4^{3-}, \downarrow PTH. - PTHrp exerts very similar physiologic effects as PTH, causing high serum calcium and low phosphate. - PTH secretion by the parathyroid glands will be suppressed in this setting due to the high serum calcium. - NBME will give you lung cancer + high serum calcium + low serum PTH, with the answer being squamous cell carcinoma of the lung. The low PTH will throw some people off. But this is not weird. PTH is not the same as PTHrp (which will be up-arrow).
Metastases	<ul style="list-style-type: none"> - \uparrow Serum Ca^{2+}, \downarrow PTH. - Once metastases seed at bony locations, cytokine activity causes lysis of the bone and release of calcium into the blood. Hypercalcemia is common in the setting of metastatic malignancies. - PTH is suppressed due to the high calcium.

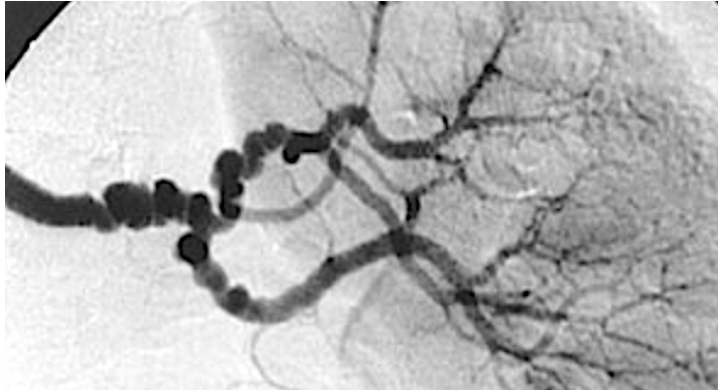
Familial hypocalciuric hypercalcemia	<ul style="list-style-type: none"> - \uparrow Serum Ca^{2+}, \downarrow urinary Ca^{2+}, \downarrow parathyroid Ca^{2+}-sensing receptor sensitivity, \downarrow renal Ca^{2+}-sensing receptor sensitivity. - As the name of the condition implies, for familial hypocalciuric hypercalcemia (FHH), serum calcium will be high and urinary calcium low. - The condition is caused by slightly decreased (not absent) sensitivity of the calcium-sensing receptors at both the parathyroid glands and kidneys, resulting in a slightly higher setpoint for calcium levels in the blood, that may be variable depending on the patient. - Most patients are asymptomatic, and PTH is often higher end of normal, or slightly elevated. Patients do not experience signs of bone resorption sometimes seen in patients with primary hyperparathyroidism. - In primary hyperparathyroidism, despite increased distal renal reabsorption of calcium, urinary calcium is still high because serum calcium is high, so more calcium will be filtered through the glomerulus. In other words, if the urine starts off with more calcium, the amount urinated out is still higher despite increased reabsorption. The calcium-sensing receptors in the renal PCT and loop of Henle function normally and can sense the high calcium, thereby decreasing paracellular reabsorption (unrelated to PTH's effect in the DCT); this allows for greater calciuresis (urination of calcium). - In familial hypocalciuric hypercalcemia, calcium-sensing receptors in the renal tubules (unrelated to PTH) have decreased sensitivity. Therefore, the tubules interpret urinary calcium to be low and will increase reabsorption in the PCT and loop of Henle to compensate, thereby decreasing calciuresis (less urinary calcium). In other words, in FHH, the kidney thinks, "Fuck, we must have low serum calcium since I can't sense it, so I goin' reabsorb more so we can retain our calcium."
PseudohypoPTH	<ul style="list-style-type: none"> \downarrow Serum Ca^{2+}, \uparrow serum PO_4^{3-}, \downarrow urinary cAMP. If the USMLE asks what change will occur with exogenous PTH administration, choose: \leftrightarrow Serum Ca^{2+}, \leftrightarrow serum PO_4^{3-}, \leftrightarrow urinary cAMP. - Pseudohypoparathyroidism is caused by a defective PTH receptor, and therefore insensitivity to PTH. - There are different types of pseudohypoparathyroidism. The USMLE will give you type I, which presents with what is referred to as the Albright hereditary osteodystrophy phenotype (i.e., shortened 4th + 5th metacarpals, round face, and bony abnormalities). Osteoma cutis (nodules of subcutaneous ossification) can be seen (on retired NBME Q). - In pseudohypoparathyroidism type I, there is no response to exogenous PTH, so we will not see any changes in serum calcium, serum phosphate, or urinary cAMP. - Normally, exogenous PTH would cause an increase in serum calcium, a decrease in serum phosphate, and an increase in urinary cAMP. - Patients with pseudohypoparathyroidism will have low serum calcium, high serum phosphate, and high serum PTH levels. That is, the calcium and phosphate levels appear as though the patient has low PTH, when in reality there is just insensitivity to it. PTH goes up due to decreased negative feedback at the calcium-sensing receptors at the parathyroid glands, since serum calcium is low.
Milk-alkali syndrome	<ul style="list-style-type: none"> - Diagnosis of exclusion on USMLE, meaning we eliminate to get there. - Textbook scenario is hypercalcemia and metabolic alkalosis (high bicarb) in someone taking too many calcium carbonate antacid tablets for GERD or dyspepsia (indigestion/upset stomach). This can lead to urolithiasis. - What the USMLE vignette will do, however, is not mention the patient's Hx, but will simply give you a kidney stone + hypercalcemia + bicarb that is elevated (or toward the upper limit of normal). Then you eliminate to get there, where you say, "Even though they don't mention the textbook presentation, no other answers explain the high calcium + high bicarb."

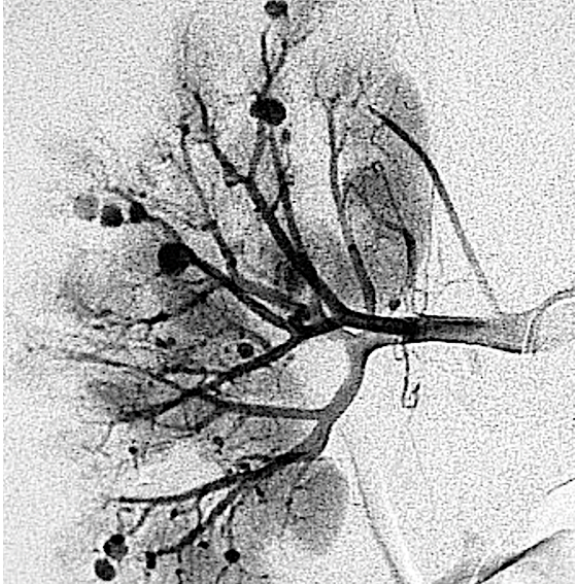
	- Normal bicarb is 22-28 mEq/L, but an NBME Q for milk-alkali syndrome gives a bicarb of 27, where this throw students off. Acid-base disorders can occasionally have bicarb in the normal range, albeit in the direction you expect.
--	---

RAAS / Adrenal hormone basics	
RAAS	<ul style="list-style-type: none"> - Renin-angiotensin-aldosterone system - ↓ Renal perfusion stimulates renin secretion from juxtaglomerular cells (JGC) of the PCT of the kidney. JGCs are modified smooth muscle cells that sense ↓ perfusion. - The liver produces a protein called angiotensinogen that is cleaved by renin in plasma into angiotensin I. - Angiotensin I goes to the lungs, where angiotensin-converting enzyme (ACE) cleaves angiotensin I into angiotensin II (AT II). - Angiotensin II has multiple roles, but one of them is to go to the zona glomerulosa of the adrenal cortex (most superficial hormone-producing layer) to upregulate aldosterone synthase, thereby ↑ aldosterone. - In other words, ↓ renal perfusion → ↑ AT II + aldosterone. - If a patient's aldosterone level is high, we look at renin (i.e., ↑ or ↓) to help us ascertain the cause of the ↑ aldosterone. - If renin and aldosterone are both ↑, we know the cause is ↓ renal perfusion. We call this renovascular hypertension, where we either have renal artery stenosis (RAS) caused by atherosclerosis (older patient with CVD risk factors) or fibromuscular dysplasia (FMD; vascular smooth muscle proliferation disorder in young women). "Reninoma" is possible but nonexistent on USMLE. - If aldosterone is ↑ but renin ↓, we know the cause of the ↑ aldosterone is primary adrenal, which means Conn syndrome (aldosterone-secreting tumor) or zona glomerulosa hyperplasia (secreting aldosterone). The ↑ aldosterone causes ↑ plasma volume, which ↑ renal blood flow, thereby ↓ renin through negative-feedback. So in short: <ul style="list-style-type: none"> - ↑ Aldosterone + ↑ renin: Renovascular hypertension (RAS or FMD). - ↑ Aldosterone + ↓ renin: Primary adrenal (Conn or hyperplasia).
Aldosterone	<ul style="list-style-type: none"> - Produced in zona glomerulosa of adrenal cortex. - Causes ↑ plasma Na^+, ↓ K^+, ↑ HCO_3^-, ↑ pH. - In other words, all of the arrows go the same direction as aldosterone except for K^+. - Aldosterone goes to the basolateral membrane (side of blood) of the cortical collecting duct in the kidney to ↑ Na^+/K^+ ATPase pumps. For every 1 ATP utilized, we get 2 K^+ secreted from the blood into the tubular cell (which ultimately leaves the body) and 3 Na^+ reabsorbed from the tubular cell into the blood. - When Na^+ is pulled out of the tubular cell into the blood, this favors a high-low gradient from the urine into the cell of sodium, causing ENaC (a sodium channel) on the apical membrane to indirectly ↑ in activity, which pulls Na^+ out of the urine. - In addition, aldosterone upregulates an H^+ ATPase on the apical membrane (side of urine) of the cortical collecting duct, causing ↑ serum HCO_3^- (i.e., ↓ plasma H^+ to mop up HCO_3^-, so HCO_3^- ↑). - The main purpose of aldosterone is to regulate fluid status in the body. Water follows Na^+, so the strong Na^+ reabsorptive effect functions to retain water. - The interesting point to note is that although ADH (vasopressin) ↑ free-water reabsorption (without pulling Na^+ in as well), this effect is more to regulate tonicity of the blood (i.e., whether plasma Na^+ is ↑ or ↓) by "diluting" out serum Na^+. Vasopressin still has some effect on volume status, but aldosterone's effect is more robust.
AT II	<ul style="list-style-type: none"> - In addition to ↑ upregulating aldosterone synthase in the zona glomerulosa of the adrenal cortex, has 3 other very important roles for USMLE: <ul style="list-style-type: none"> ○ 1) Constricts the efferent arterioles leaving the kidney.

	<ul style="list-style-type: none"> ▪ This causes \uparrow hydrostatic pressure backup at the glomerulus, which maintains GFR in the setting of \downarrow renal perfusion; this means \uparrow FF, since the latter is GFR/renal perfusion. ▪ It makes sense that AT II constricts the efferent arterioles, because when renal perfusion is \downarrow, GFR will \downarrow unless we get a “squeezing of the hose” / backup effect leaving the kidney, which functions to maintain the same glomerular filtration in spite of that \downarrow in renal blood flow. ○ 2) Constricts peripheral arterioles. <ul style="list-style-type: none"> ▪ Helps to maintain basal blood pressure. ▪ Main reason this function of AT II is HY for USMLE is because they want you to know that ACE inhibitors (e.g., lisinopril) or AT II receptor blockers (e.g., valsartan) \downarrow afterload on the heart by relieving the constrictive effects of AT II on peripheral arterioles. This promotes \uparrow ejection fraction, since there is now less force for the heart to pump against. This effect at helping to \uparrow EF, in addition to their ability to \downarrow cardiac remodeling, is why ACEi/ARBs are first-line meds in heart failure. ○ 3) Promotes Na^+ reabsorption in the PCT of the kidney. <ul style="list-style-type: none"> ▪ Contributes to fluid retention in the setting of \downarrow renal perfusion without the need for aldosterone to act distally. ▪ For example, in pre-renal azotemia, FeNa is \downarrow due to the \uparrow reabsorption of Na^+ proximally by AT II. If you’re confused by this, I discuss all of this stuff in detail in the HY Renal PDF.
Cortisol	<ul style="list-style-type: none"> - Produced in zona fasciculata of adrenal cortex. - Two most important roles for USMLE: <ul style="list-style-type: none"> ○ 1) Maintains basal BP by \uparrow α_1-receptor expression on peripheral arterioles. Norepinephrine and epinephrine (catecholamines produced in adrenal medulla) then bind to α_1-receptors, causing arteriolar constriction and \uparrow BP. ○ 2) Maintains basal blood glucose levels by \uparrow insulin resistance at peripheral tissues (physiologic/healthy if cortisol levels are normal) and \uparrow gluconeogenesis. ○ 3) For repro/obgyn, it also accelerates fetal lung maturity by \uparrow surfactant production by the lamellar bodies within type II pneumocytes. - ACTH causes cortisol secretion by the zona fasciculata of the adrenal cortex. - Cortisol will then induce negative-feedback at the hypothalamus and anterior pituitary to \downarrow CRH and ACT, respectively. - If cortisol is \downarrow, CRH and ACTH go \uparrow due to lack of negative-feedback. - The precursor to ACTH is proopiomelanocortin (POMC), which is cleaved into both ACTH as well as α-MSH (melanocyte-stimulating hormone). - \downarrow cortisol causing \uparrow CRH \rightarrow \uparrow POMC \rightarrow \uparrow ACTH + \uparrow α-MSH is why hyperpigmentation is seen in Addison disease.

Renovascular hypertension	
Renal artery stenosis (RAS)	<ul style="list-style-type: none"> - Narrowing of one or both renal arteries due to atherosclerosis that causes \uparrow renin-angiotensin-aldosterone system (RAAS) and \uparrow BP. - Q will be patient over the age of 50 with cardiovascular disease risk factors, such as diabetes, HTN, and/or smoking. - Patients who have pre-existing HTN causing atherosclerosis leading to RAS will often have 10-20 years of background HTN that then <i>becomes accelerated</i> over a few-month to 2-year period. What this means is: the slowly developing atherosclerosis in the renal arteries finally reaches a point at which the kidney is unable to maintain autoregulation, and the RAS is now clinical (i.e., accelerated HTN of $\uparrow\uparrow$ BP within, e.g., 3 months).

	<ul style="list-style-type: none"> - Another way USMLE will give RAS is by giving \uparrow BP in patient with significant evidence of atherosclerotic disease (i.e., Hx of coronary artery bypass grafting, intermittent claudication), and then ask for the most likely cause \rightarrow RAS. You have to say, "Well he clearly has atherosclerosis in his coronaries and aortoiliac vessels, so that means he'll have it in the renal arteries too." - Q can say older patient with carotid bruit has recent $\uparrow\uparrow$ in BP and then ask for diagnosis \rightarrow answer = RAS. Similar to above, if the patient has atherosclerosis in one location (i.e., the carotids), then he/she will have it elsewhere too. - HY factoid about RAS is that ACEi or ARBs will cause renin and/or creatinine to go up. This is a HY point that is often overlooked and is asked on NBMEs. I have not seen NBME care whether it's uni- or bilateral in this case. \rightarrow Kidney can autoregulate across flux in perfusion. Patients with already-compromised renal blood flow are more sensitive to the subtle \downarrow in filtration fraction that occurs secondary to ACEi/ARB use, so renin/creatinine \uparrow. - If USMLE gives you unilateral RAS, renin is only \uparrow from that kidney. The other kidney will not produce \uparrow renin. - After renin and aldosterone levels are obtained, MR angiography of the renal vessels is what USMLE wants for the next best step in diagnosis.
Fibromuscular dysplasia (FMD)	<ul style="list-style-type: none"> - The answer on USMLE for narrowing of the renal arteries in a woman 20s-40s. - Not the same as renal artery stenosis, and not caused by atherosclerosis. - If you broadly say "renal artery stenosis," that specifically refers to atherosclerosis of the renal arteries in patient >50 with CVD. - FMD is tunica media hyperplasia (not dysplasia, despite the name) that results in a "string of beads" appearance on renal angiogram.  <ul style="list-style-type: none"> - MR angiography is answer on NBME for diagnostic modality. - Can affect the carotid vessels. A 2CK Surg Q gives FMD vignette and also says there is 25% occlusion of one of the carotids.
Polyarteritis nodosa (PAN)	<ul style="list-style-type: none"> - As discussed in the cardio PDF, this is a medium-vessel vasculitis that causes a "string of pearls" appearance of the renal vessels. This can be confused with FMD, but note the difference in the imaging. FMD shows more beading along the larger/proximal arterial sections, whereas PAN shows pearls more at the vascular termini, with the more proximal parts more likely to be spared.

	 <p>Angiogram of PAN shows pearls that are more distal in the renal vasculature; FMD, in contrast, shows more proximal beading, with the termini not as conspicuously involved.</p> <ul style="list-style-type: none"> - There is an NBME Q where they list both PAN and FMD as answer choices and it relies on you knowing the angiogram to get it right. They don't mention hepatitis B, but answer is PAN. That's why I'm harping on this here. - Causes fibrinoid necrosis. - Can be caused by hepatitis B. - Sparing the pulmonary vasculature.
Renal artery thrombosis	<ul style="list-style-type: none"> - The answer on USMLE for hypertension in a neonate following umbilical artery catheterization. USMLE simply wants "\uparrow renin, \uparrow aldosterone" as the answer. - Sounds weird, but you need to know umbilical artery catheterization is a major risk factor for renal artery thrombosis in neonates. - 2CK NBME Q gives brief umbilical artery catheter insertion in kid born 26 weeks' gestation in order to monitor blood pressure for a pneumonia. 3 weeks later, he has \uparrow BP (128/86) \rightarrow answer = "\uparrow renin, \uparrow aldosterone" as answer. - BP in term neonates should be \sim60/40. In a preemie 29 weeks' gestation, it should be \sim50/30.

Primary adrenal DDx affecting aldosterone	
Conn syndrome	<ul style="list-style-type: none"> - Aldosterone-secreting tumor. - Causes \uparrow Na^+, \downarrow K^+, \uparrow HCO_3^-, \uparrow pH. - Renin is \downarrow due to negative-feedback at the kidney. In other words, the \uparrow aldosterone from the tumor \uparrow fluid retention, which causes \uparrow renal blood flow, which shuts off renin production. - In \sim50% of aldosterone-derangement Qs, Na^+ will be normal. This confuses students, but it's because the body has strong ability to maintain Na^+ (i.e., also via ADH). - Tx = spironolactone (aldosterone receptor antagonist) prior to surgery.
Familial hyperaldosteronism	<ul style="list-style-type: none"> - There are gene mutations that can cause \uparrow primary adrenal production of aldo. - If the USMLE gives you Q where various family members have \uparrow BP + \uparrow aldosterone and they don't tell you any other info, including the renin level, the answer is primary hyperaldosteronism, not renovascular hypertension (i.e., FMD or RAS). - There is a Q on a 2CK NBME form where they do this, and the student says, "But wait, how are we supposed to know it's primary and not FMD/RAS?" It's because if \uparrow

	aldo is familial, it's likely due to gene mutations causing \uparrow primary production from the zona glomerulosa.
Addison disease	<ul style="list-style-type: none"> - Autoimmune destruction of the adrenal cortex, leading to \downarrow aldosterone <i>and</i> \downarrow cortisol. - I haven't seen the USMLE ever care about "decreased androgens," so the effect is predominantly on the zona glomerulosa and fasciculata. - Called "primary adrenal insufficiency" because the adrenal gland itself is under-producing hormones. - Addison is idiopathic / can be seen in patients with Hx of other autoimmune diseases, either in themselves or family members (i.e., the vignette throws in the side-detail that the brother has RA, or the sister has IBD, or the patient has Hx of thyroiditis). - \downarrow Na⁺, \uparrow K⁺, \downarrow pH, \downarrow bicarb. - Blood pressure will either be low-normal or low, due to both \downarrow aldosterone as well as \downarrow cortisol. I explicate this because students tend to just mention the \downarrow aldosterone as the reason BP is \downarrow, but the effect of \downarrow cortisol is HY for USMLE. - ACTH and α-MSH are both \uparrow due to \downarrow cortisol \rightarrow hyperpigmentation. Although I'd say they only mention this in ~50% of vignettes. - Patients can present with eosinophilia. This is because cortisol normally plays a role in helping to sequester eosinophils within the spleen + facilitates eosinophil apoptosis, so \downarrow cortisol means \uparrow eosinophils. Don't go chasing stool ova and parasites. Qs can give you eosinophils of 15-25%, where you're like wtf? They should normally be <5%. - Classic Addison vignette is patient (young or old, I've seen both) who has ongoing fatigue + hyperpigmentation, and then the answer is just "ACTH stimulation test." - Exogenous ACTH should normally cause a robust $\uparrow\uparrow$ in cortisol from the adrenal fasciculata. In the setting of primary adrenal insufficiency, since the adrenal gland is fucked up, giving exogenous ACTH won't do jack shit. - \downarrow cortisol causes chronic fatigue syndrome. This is one of the most over-looked details in NBME Qs and in real life. Any time a patient has ongoing chronic fatigue that is unexplained, cortisol levels should be checked. If they are \downarrow, hydrocortisone will immediately boost the patient. - Tx for Addison = fludrocortisone +/- hydrocortisone. Fludrocortisone is a mineralocorticoid similar to aldosterone. Hydrocortisone is a glucocorticoid similar to cortisol.
Waterhouse-Friderichsen	<ul style="list-style-type: none"> - Meningococcal septicemia causing bilateral hemorrhagic necrosis of the adrenal glands, resulting in \downarrow aldosterone and \downarrow cortisol. - Vignette will be \downarrow BP + \downarrow Na⁺ + \uparrow K⁺ + \downarrow bicarb in patient with meningococcal infection (e.g., recent meningitis + non-blanching rash), where answer = ACTH stimulation test.

Adrenal crisis

- Patients who are on chronic glucocorticoids (i.e., prednisone) for autoimmune conditions such as IBD, RA, SLE, etc., will have a chronically suppressed adrenal gland that is atrophied, since prednisone is a cortisol analogue that induces negative-feedback and shuts off ACTH production.
- This means that if these patients encounter a stressor such as surgery, trauma, infection, or thyroid storm, where glucocorticoids normally experience \uparrow rate of consumption, they are unable to "mount a stress response," (i.e., unable to produce an acute \uparrow production of cortisol), so they are prone to acute glucocorticoid deficiency and a precipitous $\downarrow\downarrow$ in BP.
- Q will tell you patient has SLE treated with prednisone who goes into surgery and gets a $\downarrow\downarrow$ drop in BP to 80/40 + fluids and pressors don't help; Q asks next best step \rightarrow answer = IV hydrocortisone or methylprednisolone. What we are doing is replenishing the glucocorticoid. "Pressors" can refer to NE, E, or even desmopressin.

- Remember that without cortisol (or cortisol equivalent, i.e., exogenous glucocorticoid), we can't get adequate α_1 -receptor expression on arterioles, so even if NE and E are floating around in normal amounts (or given exogenously), they can't bind to α_1 -receptors to maintain BP.
- This concept is referred to as: "glucocorticoids are permissive of the effects of catecholamines," where they literally "permit" NE and E to do their job.
- The Q can also tell you patient being treated with prednisone for SLE or RA experiences an acute thyroiditis (remember autoimmune diseases go together) and gets $\downarrow\downarrow$ in BP \rightarrow answer = hydrocortisone (after fluids). Or patient with autoimmune disease gets an infection + $\downarrow\downarrow$ in BP \rightarrow answer = hydrocortisone (after fluids).

Cushing syndrome vs disease

- **Cushing syndrome** = how the patient looks/presents; can refer to any cause of Cushingoid presentation (i.e., exogenous glucocorticoids, ACTH-secreting tumor of anterior pituitary, cortisol-secreting tumor of adrenal cortex, small cell bronchogenic carcinoma secreting ACTH).
- **Cushing disease** = only ACTH-secreting tumor of anterior pituitary.
- If patient walks through the door and appears Cushingoid due to an ACTH-secreting tumor of the anterior pituitary, we would say, "The patient has Cushing syndrome caused by Cushing disease."
- Highest yield findings for Cushingoid appearance on USMLE, as per my observation, are: **purple striae** on the abdomen / stretch marks, **osteoporosis** (compression fractures of vertebrae), and **avascular necrosis of the femoral head** (hip pain). Findings such as buffalo hump, moon facies, central obesity, peripheral muscle wasting, hypertension, and diabetes type II are important and pass-level, but you really need to know those 3 bold findings I write above.
- In Peds, Cushings can present as precocious puberty without all of the classic findings.
- Chronically elevated cortisol can cause **hypokalemia** similar to high aldosterone. Sometimes NBME will give you a vignette of Cushings + mention potassium is 3.0 mEq/L (NR 3.5-5.0), and you're like, "why the fuck is the potassium low. Is aldosterone high?" No. All glucocorticoids have some degree of mineralocorticoid effect at the kidney similar to aldosterone. In patients who have high cortisol, the effect longer term can occasionally cause hypokalemia. This detail is particularly important for 2CK vignettes.

Dexamethasone suppression test

- Dexamethasone is a cortisol analogue that is capable of exerting negative-feedback at the hypothalamus and anterior pituitary. Given to healthy individuals, the result is suppression of ACTH and cortisol levels.
- The dexamethasone suppression test is done to determine the etiology of *endogenous* Cushing syndrome (i.e., the patient isn't taking exogenous steroids). This is because if the patient is taking steroids, clearly we know the cause of the Cushings already.
- Low-dose dex will suppress ACTH and cortisol in healthy patients. It is effectively a "yes or no" test for Cushing syndrome, where if there's suppression of cortisol with low-dose dex, then we can say, "Patient doesn't have Cushings"; if cortisol doesn't suppress, then we know the patient has Cushings, but we just don't know the cause yet.
- High-dose dex helps us differentiate Cushing disease from other causes of Cushing syndrome. This is because only Cushing disease will have suppressed cortisol levels.
- Therefore, if cortisol goes \downarrow with high-dose dex, we know the diagnosis is Cushing disease.
- If cortisol does not go \downarrow with high-dose dex, we look at ACTH level.
- If ACTH is \downarrow , we say, the only way that possible to have \uparrow cortisol with \downarrow ACTH is if the diagnosis is an adrenal cortical adenoma of the zona fasciculata secreting cortisol.
- If ACTH is \uparrow , we know the cause is ectopic ACTH secretion from small cell bronchogenic carcinoma. The reason we know the ACTH isn't from the pituitary is because high-dose Dex didn't suppress cortisol.

Cushing disease

- \uparrow ACTH + \uparrow cortisol.
- Suppresses with high-dose dex.
- If high-dose dex is given and they ask for the arrows for how ACTH and cortisol *will change*, the answer is " \downarrow ACTH, \downarrow cortisol."

Small cell lung cancer	<ul style="list-style-type: none"> - \uparrow ACTH + \uparrow cortisol. - Does not suppress with high-dose dex. - If high-dose dex is given and they ask for the arrows for how ACTH and cortisol <i>will change</i>, the answer is “no change ACTH, no change cortisol.”
Adrenal adenoma	<ul style="list-style-type: none"> - \downarrow ACTH + \uparrow cortisol. - Does not suppress with high-dose dex. - Same as with small cell lung cancer, if high-dose dex is given and they ask for the arrows for how ACTH and cortisol <i>will change</i>, the answer is “no change ACTH, no change cortisol.”
Exogenous steroids	<ul style="list-style-type: none"> - \downarrow ACTH + \downarrow cortisol (holy shit). - Exogenous steroids (i.e., prednisone, hydrocortisone) are not the same thing as cortisol. The result is suppression of endogenous cortisol. - Students get this wrong all of the time.

Miscellaneous	
Glucocorticoid psychosis	<ul style="list-style-type: none"> - Glucocorticoids can cause “glucocorticoid psychosis,” which can present as an overt psychosis, delirium-like presentation, or even just as general mood disturbance, i.e., depression. - The vignette can give you Cushing syndrome + depression, or recent IV methylprednisolone injection + delirium-like presentation 24-48 hours later.
Licorice	<ul style="list-style-type: none"> - Licorice contains glycyrrhizic acid, which leads to \uparrow mineralocorticoid effect, at the kidney (i.e., similar to aldosterone). - Can cause hypokalemia in those who drink excessive licorice tea.

Catecholamine-secreting tumors	
Pheochromocytoma	<ul style="list-style-type: none"> - Catecholamine-secreting tumor of adrenal medulla. - Derived from neural crest (i.e., chromaffin cells of adrenal medulla). - Occurs in adults; can calcify. - Causes paroxysmal (i.e., comes and goes) $\uparrow\uparrow$ BP, which presents as periodic palpitations and pounding headaches. - Because the HTN is paroxysmal, the patient can have BP measured in the office at 120/80, so do not exclude pheo in this case. - Stressors (e.g., sitting up on the examination table) can trigger \uparrow NE + E release from the tumor, where BP shoots up to $>180/100$. This is different from whitecoat hypertension, where young patient has 140/90 measured due to being slightly nervous. - Diagnose with urinary/serum metanephrines. If positive, then do CT abdomen. - Tx = phenoxybenzamine (irreversible α1-blocker). If you give beta-blocker first, this will kill the patient. This is because if you block beta receptors, the NE and E have little to bind to now except α receptors (mainly α1), so we get $\uparrow\uparrow$ arteriolar constriction and BP shoots up. This is called “unopposed alpha.” - Some students ask about giving propranolol after phenoxybenzamine. The answer is, yes, in theory this can be done. But USMLE doesn’t assess this. They want straight-up alpha-blockade. - Pheo can be idiopathic or part of condition such as MEN 2A/B or NF1. - If a patient has medullary thyroid cancer, you must check for pheochromocytoma before doing thyroidectomy. This is because if the patient has MEN 2 and you don’t check for pheo first, doing surgery will cause $\uparrow\uparrow$ BP due to catecholamine release and kill the patient.
Neuroblastoma	<ul style="list-style-type: none"> - Essentially the “pediatric pheo”; <i>N-myc</i> gene. - Secretes catecholamines; can calcify (same as pheo in adults).

	<ul style="list-style-type: none"> - Grows from the median (midline) sympathetic chain. Usually intra-abdominal but can sometimes be in the posterior mediastinum. Sounds odd, but the latter shows up on a 2CK form. - Causes \uparrow BP and findings such as opsoclonus-mycoclonus syndrome (dancing eyes) and violaceous eyelids (sounds like heliotrope rash of dermatomyositis but unrelated). - Diagnose with urinary homovanillic acid (HVA) and vanillylmandelic acid (VMA), which are metabolites of catecholamines. - Metaiodobenzylguanidine scan can be done after HVA and VMA detected.
--	--

Congenital adrenal hyperplasia (CAH)	
<p>- Autosomal recessive.</p> <p>- 21-, 11-, and 17-hydroxylase deficiencies. 21-hydroxylase deficiency is most common.</p> <p>- ACTH is \uparrow in all three types. This is the mechanism USMLE wants for the hyperplasia. That is, cortisol production is impaired in all three, so ACTH goes \uparrow to compensate \rightarrow stimulates hyperplasia of adrenals.</p> <p>- The USMLE will give a vignette of CAH, followed by "which of the following is the most likely explanation for these findings?" \rightarrow answer = "Increased ACTH secretion." Sounds weird, but it's on NBME.</p> <p>- The relevance of these conditions is that they are a cause of ambiguous genitalia and/or virilization.</p> <p>- Presentations are variable, with Qs giving vignettes in neonates, children, and adults. So the way to differentiate them comes down to electrolytes and BP.</p> <p>- For both 21- AND 11-hydroxylase deficiencies:</p> <ul style="list-style-type: none"> o \uparrow 17-OH substrates (i.e., 17-OH-progesterone and 17-OH-pregnenolone). o \uparrow DHEA-S, \uparrow androstenedione. o If you see any of these up in the Q, you know right away answer is either 21- or 11-deficiency. This is because it's impossible to get 17-OH substrates in 17-hydroxylase deficiency. 	
<pre> graph TD A["17-OH substrates, DHEA-S, and/or androstenedione \uparrow?"] -- No --> B["Dx = 17-OH deficiency"] A -- Yes --> C["Dx = 21- or 11-OH deficiency"] C -- "K^+ \uparrow or BP \downarrow/normal" --> D["Dx = 21-OH deficiency"] C -- "K^+ \downarrow/normal or BP \uparrow" --> E["Dx = 11-OH deficiency"] </pre>	
21-hydroxylase deficiency	<ul style="list-style-type: none"> - \uparrow Serum K^+, \downarrow Na^+, \downarrow pH, \downarrow HCO_3^-, \downarrow glucose. - $\downarrow/\leftrightarrow$ BP. - Cortisol and aldosterone, as well as their precursors, are all low.
11-hydroxylase deficiency	<ul style="list-style-type: none"> - $\downarrow/\leftrightarrow$ Serum K^+, \uparrow/\leftrightarrow Na^+, \uparrow/\leftrightarrow pH, \uparrow/\leftrightarrow HCO_3^-, \uparrow/\leftrightarrow glucose. - \uparrow BP. - Cortisol and aldosterone are low, but their precursors, which have some effect, are high.
17-hydroxylase deficiency	<ul style="list-style-type: none"> - \downarrow 17-OH substrates (i.e., 17-OH-progesterone and 17-OH-pregnenolone) - \downarrow DHEA-S, \downarrow androstenedione - \downarrow Serum K^+, \uparrow Na^+, \uparrow pH, \uparrow HCO_3^- (high aldosterone) - \downarrow glucose (cortisol and its precursor are low).

Carcinoid tumor	
<ul style="list-style-type: none"> - Neuroendocrine tumor of small bowel, appendix, or lung that is S-100 (+) and consists of small blue cells. - Secretes serotonin. - Presents as flushing, tachycardia, diaphoresis, and diarrhea. - Tricuspid regurg common (holosystolic murmur that increases with inspiration) due to tricuspid lesions. - Diagnose with urinary 5-hydroxyindole acetic acid (5-HIAA). - Don't confuse with serotonin syndrome, which is a drug interaction (e.g., starting a monoamine oxidase inhibitor too soon after discontinuing an SSRI, or if a patient takes St John wort with an SSRI). 	

Polyglandular syndromes	
- All MEN syndromes and Carney complex are autosomal dominant.	
MEN 1	<ul style="list-style-type: none"> - <i>MEN1</i> gene mutation. - Parathyroid adenoma (or hyperplasia), pituitary adenoma, pancreatic adenoma. <ul style="list-style-type: none"> o Zollinger-Ellison syndrome (gastrinoma) is highest yield pancreatic tumor in MEN 1. Will present as recurrent peptic ulcers. I discuss this stuff in detail in the HY Gastro PDF. o Parathyroid adenoma often presents with calcium urolithiasis, where they will mention flank or groin pain in patient with Hx of ulcers (Zollinger-Ellison). o Prolactinoma is highest yield pituitary tumor. o USMLE need not give the full constellation of findings for the MEN syndromes. There is an NBME Q floating around where the patient has a parathyroid adenoma – nothing more – and the answer is just <i>MEN1</i> as the gene that's mutated.
MEN 2A	<ul style="list-style-type: none"> - <i>RET</i> proto-oncogene mutation. - Parathyroid adenoma (or hyperplasia), pheochromocytoma, medullary thyroid carcinoma. <ul style="list-style-type: none"> o As mentioned earlier, <i>RET</i> mutations need not cause the full constellation of findings. NBME Qs can give isolated medullary thyroid carcinoma in a family, and the answer is just <i>RET</i>. o In theory, isolated parathyroid adenoma could also be <i>RET</i>, but with the NBME example I mentioned above they listed <i>MEN1</i> without also listing <i>RET</i>.
MEN 2B	<ul style="list-style-type: none"> - <i>RET</i> proto-oncogene mutation. - Marfanoid body habitus, mucosal neuromas, pheochromocytoma, medullary thyroid carcinoma. <ul style="list-style-type: none"> o -Oid means looks like but ain't. So the patient might look like he/she has Marfan's (i.e., tall, lanky) but doesn't, because this isn't <i>FBN1/2</i> mutation. o As mentioned earlier, before doing thyroidectomy for medullary thyroid carcinoma, you must check for pheochromocytoma (because stress of surgery will ↑↑ catecholamines from the tumor and kill the patient) by first doing urinary metanephrines. If positive, then do CT of the abdomen.
Carney complex	<ul style="list-style-type: none"> - Hyperpigmentation, atrial myxoma, endocrine hypersecretion. <ul style="list-style-type: none"> o The hyperpigmentation can present as perioral melanosis (i.e., hyperpigmentation around the lips/mouth) that sounds similar to Peutz-Jegher syndrome, but instead of the Q focusing on hamartomatous colonic polyps, they mention a cardiac tumor and another endocrine organ hyper-secreting. And you're like huh? o Atrial myxoma normally shows up in adults; cardiac rhabdomyoma normally shows up in children with tuberous sclerosis. In Carney, the Q can say atrial myxoma <i>in a kid</i>. So it's the only example on USMLE that breaks the rule. o Endocrine hypersecretion is classically Cushing syndrome (granular hyperpigmentation of the zona fasciculata) or hyperthyroidism. o The reason you likely haven't heard of Carney complex before is because students coming out of the USMLE didn't even realize this is what they saw.

Diabetes mellitus (DM)	
<ul style="list-style-type: none"> - The word diabetes means polydipsia + polyuria (i.e., drinking a lot and peeing a lot). - I see students frequently misconstrue diabetes mellitus with diabetes insipidus, since both vignettes will give patients who have increased thirst and urination. - A key detail that distinguishes acute diabetes mellitus from diabetes insipidus is that DM vignettes can often mention weight loss due to \uparrow catabolism. Weight loss is also seen in acute type II, even though the patient is usually overweight. Vomiting is another HY finding in acute DM. - So if vignette says \uparrow thirst + \uparrow urination + weight loss +/- vomiting, this is DM, not DI. - For extensive info on the effects of diabetes on different organ systems (i.e., cardio, renal, ophthal, GIT, pregnancy, etc.), go to those corresponding chapters of this document. I will keep the focus in this table on endocrine and electrolytes / acid-base. - Diagnosis of DM is made by measuring two fasting glucoses >126 mg/dL, any one random fasting glucose >200 mg/dL, or an HbA1c of $>6.5\%$. 	
Type I	<ul style="list-style-type: none"> - Absence of insulin; autoimmune-mediated; no one specific gene, although HLA-DR3/4 are associated. - Often described as “genetic susceptibility with environmental trigger” (i.e., viral infection, usually Coxsackie B). - Occurs almost always in children or teenagers of normal BMI. - Pathogenesis is usually combo of an antibody- (anti-GAD65 or -ZnT8) and T-cell-mediated process that leads to destruction of β-islet cells in the tail of the pancreas \rightarrow \downarrow insulin secretion \rightarrow inability to recruit GLUT4 to cell surface of skeletal muscle and adipose tissue \rightarrow inability to take up glucose into cells \rightarrow cells are starved of energy \rightarrow \uparrow gluconeogenesis + ketogenesis. - Hyperglycemia occurs as a result of continued glucose production by the liver (gluconeogenesis) in combination with \downarrow uptake by skeletal muscle and adipose tissue. - Biopsy of pancreas shows inflammatory infiltrate in acute type I DM; in late type I (i.e., years later), it shows atrophy and fibrosis. - It is the absence of insulin in type I DM that enables ketogenesis. In type II DM, ketones are low, not high, because insulin is present. - Ketone bodies (USMLE likes β-hydroxybutyrate) are highly acidic, so will drop the blood pH (high anion-gap metabolic acidosis). - Vignette will give kid or teenager with polyuria, polydipsia, and sometimes vomiting, who has severe metabolic acidosis (bicarb \downarrow), which is due to diabetic ketoacidosis. Breath can be fruity in odor (smell of ketones). DKA will have: <ul style="list-style-type: none"> - \downarrow pH, \downarrow HCO_3^-, \downarrow CO_2. <ul style="list-style-type: none"> - Ketone bodies are acidic \rightarrow causes metabolic acidosis (decreased bicarbonate). - CO_2 is acidic, so we blow that off to compensate. Kussmaul breathing is deep, labored breathing seen in DKA. - \uparrow β-hydroxybutyrate, \uparrow serum osmolality, \uparrow anion gap. <ul style="list-style-type: none"> - β-hydroxybutyrate is a ketone body. Since we have ketosis (ketone production), it will be increased. - Serum osmolality is increased because serum glucose is markedly increased (insulin isn't present to drive glucose into cells). Even though serum sodium is low (so you might think osmolality is low similar to SIADH), the \uparrow glucose makes serum osmolality high. - DKA is the D in MUDPILES, so anion gap is up. - \downarrow Serum Na^+, \uparrow serum K^+, \downarrow total body K^+, \uparrow GFR. <ul style="list-style-type: none"> - Serum sodium is decreased mostly due to dilutional hyponatremia. As mentioned earlier, serum osmolality is high, which causes fluid retention intravascularly \rightarrow dilutes out serum sodium. In addition, low insulin means less glucose enters cells \rightarrow less ATP production \rightarrow less cellular Na^+/K^+-ATPase activation \rightarrow sodium not pumped out of cells. - We describe the state of K^+ as: hyperkalemia (high serum K^+) despite a low total body potassium. - Serum potassium is high for two main reasons: <ol style="list-style-type: none"> 1) Potassium-proton shift: Acidosis (due to ketosis) causes protons in the blood to exchange with potassium in the cell via the H^+/K^+-antiporter (i.e., H^+ goes into cell; K^+ moves out).

	<p>2) Insulin drives potassium into cells (and we don't have insulin in DKA): Insulin normally leads to the upregulation of a Na^+/K^+-ATPase antiporter that moves 3Na^+ out for every 2K^+ in. If insulin is low, then less K^+ will be moved into the cell → hyperkalemia (high potassium in blood).</p> <ul style="list-style-type: none"> - Total body potassium is low because of increased losses at the kidney. Since serum potassium is high, more potassium is filtered through the glomerulus, so more is excreted (i.e., the kidney thinks there's too much potassium in the body since more is being filtered, so it tries to get rid of more of it). However, this causes bodily depletion of K^+ because the processes that cause hyperkalemia are unmitigated, so the kidney continues to excrete potassium. - GFR is increased because of hyperfiltration secondary to hyperglycemia. That is, since serum glucose is high, more glucose is filtered through the glomerulus, which pulls water with it → hyperfiltration. - Tx for DKA is normal saline first (i.e., 0.9% NaCl), prior to giving insulin. - Serum potassium will drop as insulin is given. If the Q tells you patient has DKA + shows you normal potassium (even though it's usually high) + insulin is given + patient now has arrhythmia, the answer is potassium for which electrolyte is disturbed (i.e., potassium was normal prior to giving insulin, but now it's been driven into cells and the patient's developed hypokalemia). - Bicarb is always a wrong answer for low pH in DKA. - Don't confuse DKA with a hypoglycemic episode. The latter will be a type I diabetic who went out to do exercise or who was cleaning the roof of his house, who is now found unconscious → if insulin dose is not decreased prior to exercise, patient can get hypoglycemia. The Tx is intramuscular glucagon (2CK likes this) or dextrose in water. - Sometimes the USMLE can give a bit of a weird Q where they say a patient is given insulin for diabetes but has prolonged hypoglycemia + they ask why → answer = "deficiency of counter-regulatory glucagon." You need to know that in advanced diabetes, the glucagon-producing α-islet cells of the pancreas can also get fucked up. I've also seen this Q asked for chronic alcoholism and pancreatectomy; in both cases, if insulin is given, prolonged hypoglycemia can result from "deficiency of counter-regulatory glucagon."
Type II	<ul style="list-style-type: none"> - Insulin resistance; seen usually in high-BMI adults, but can rarely show up in Peds (2CK form gives type II in a 17-yr-old). - High BMI causes insulin resistance because adipose tissue secretes adipokines that impair insulin signaling. - Insulin is <i>high</i> initially (hyperinsulinemia) due to β-cell hypertrophy in order to compensate for peripheral insulin resistance. - Ketones are absent/low because the presence of insulin inhibits ketogenesis. - The two above points are the highest yield pieces of info for USMLE. - Biopsy of the pancreas initially shows β-cell hypertrophy, but years later will show amyloid deposition and cell shrinkage. - Same as with type I, hyperglycemia occurs as a result of continued glucose production by the liver (gluconeogenesis) in combination with ↓ uptake by skeletal muscle and adipose tissue. - Hyperosmolar hyperglycemic state (HHS) is seen in type II; DKA is strictly type I on USMLE. - In HHS, glucose is usually >600 mg/dL (in DKA, it need not be this high) and bicarb is usually not below 20 mEq/L (NR 22-28); in DKA, bicarb can be as low as it wants (I've seen 5 mEq/L on NBME). - The USMLE vignette will give massive paragraph Q where they mention glucose is 700 and then ask for the cause of mental status change → answer = "hyperosmolality," or simply "hyperglycemia," or "osmotic diuresis" (causes severe dehydration). I point this out because this is particularly prevalent on 2CK NBMEs, where they'll give a 15-line bullshit paragraph with tons of lab values that the student spends 9 minutes reading, but meanwhile you can see glucose is 650 and then the answer is just "osmotic diuresis" or "hyperosmolality"; should take two seconds to answer. - Mental status change is technically due to hyperosmolality in the ECF of the brain pulling water out of the ICF (i.e., the cells).

	<ul style="list-style-type: none"> - Treat HHS with normal saline first prior to insulin. - I discuss the various meds for type II diabetes later in this PDF.
Other causes	<ul style="list-style-type: none"> - Hereditary hemochromatosis ("bronze diabetes") → iron deposition in tail of the pancreas, leading to impaired fasting glucose / overt diabetes. Hyperpigmentation is due to hemosiderin deposition. Patients can also get cardiomyopathy, infertility, and pseudogout. - Cushing syndrome (as discussed earlier) can cause diabetes due to the insulin resistance caused by glucocorticoids. - Acromegaly (growth hormone causes insulin resistance). - Alcoholism can cause chronic pancreatitis that not only leads to exocrine pancreatic burnout and steatorrhea, but can also cause diabetes due to loss of islet cells. - Pancreatectomy is self-explanatory. If you remove some of the tail of the pancreas, this can lead to diabetes. - Tacrolimus is a HY drug that can cause diabetes. Other drugs can do this, but tacrolimus is the notable one for USMLE. Tacrolimus is an immunosuppressant that ↓ IL-2 synthesis and T cell stimulation.

Electrolytes	
Calcium	<ul style="list-style-type: none"> - 8.4-10.2 mg/dL. - Low Ca causes "up" presentation of tetany and hyperreflexia; high Ca causes "down" presentation of muscle flaccidity and hyporeflexia; high Ca also associated with delirium/confusion (hypercalcemic crisis). - High calcium HY causes are sarcoidosis (due to ↑ vitamin D), primary hyperparathyroidism (adenoma, hyperplasia, MEN 1/2A), metastatic malignancy, multiple myeloma, and thiazides (cause - Ca reabsorption in DCT). - Low calcium HY causes are rickets/osteomalacia (↓ vitamin D), secondary hyperparathyroidism (renal failure), post-thyroidectomy (concomitant loss of parathyroids), DiGeorge syndrome (agenesis of 3rd and 4th pharyngeal pouches), and loop diuretics (↓ paracellular reabsorption), hypomagnesemia (hypo-Mg can cause hypo-Ca and hypo-K non-responsive to supplementation; usually seen in alcoholics).
Sodium	<ul style="list-style-type: none"> - 135-145 mEq/L. - Sodium derangement (high and low) causes CNS dysfunction – i.e., confusion, stupor, or coma. - Na can often be normal in USMLE vignettes despite your expectation that it might be characteristically deranged – e.g., patient has Conn syndrome and yet the sodium is normal, and you're like wtf? (because you expect it to be elevated); this is typical for USMLE vignettes. - High Na HY causes are primary hyperaldosteronism, renal artery stenosis, fibromuscular dysplasia, dehydration, diabetes insipidus. - Low Na HY causes are Addison disease, psychogenic polydipsia, SIADH.
Potassium	<ul style="list-style-type: none"> - 3.5-5.0 mEq/L. - Potassium derangement (high and low) causes cardiac dysfunction → arrhythmia (contrast this with Na, which causes CNS dysfunction). - High K HY causes are Addison disease, renal failure, polypharmacy with agents such as potassium-sparing diuretics and digoxin. - Low K HY causes are primary hyperaldosteronism, renal artery stenosis, fibromuscular dysplasia, Cushing disease (chronically high glucocorticoid levels can cause hypo-K due to distal renal secretion similar to mineralocorticoids), vomiting, diarrhea, loop diuretics and thiazides, and hypomagnesemia (hypo-Mg can cause hypo-K and hypo-Ca non-responsive to supplementation; usually seen in alcoholics).
Phosphate	<ul style="list-style-type: none"> - 2.5-4.5 mg/dL. - High phosphorus HY causes are hypoparathyroidism, secondary hyperparathyroidism, renal failure, tumor lysis syndrome, and sarcoidosis (↑ vitamin D). - Low phosphorus HY causes are primary hyperparathyroidism, rickets / osteomalacia, and refeeding syndrome.

Magnesium	<ul style="list-style-type: none"> - 1.7-2.2 mg/dL. - Magnesium derangement causes effects similar to Ca – i.e., low Mg presents with an “up” state of hyperreflexia and increased muscle tone; high Mg presents with a “down” state of hyporeflexia and muscle flaccidity. - Low Mg HY cause is alcoholism (decreased dietary intake); leads to hypocalcemia and hypokalemia non-response to supplementation.
-----------	---

Acid/base	
(If you want practice with acid/base USMLE Qs and/or are confused by certain things I list in this table, go through my HY Arrows PDF. I discuss this stuff in comprehensive detail).	
<ul style="list-style-type: none"> - Normal blood pH: 7.35-7.45. - Normal blood HCO₃⁻: 22-28 mEq/L. - Normal blood pCO₂: 33-44 mmHg. 	
Metabolic acidosis	- Low pH caused by low HCO ₃ ⁻ ; pCO ₂ will go down to compensate (CO ₂ is acidic).
High anion-gap metabolic acidoses	<ul style="list-style-type: none"> - MUDPILES is mnemonic for high-anion-gap metabolic acidoses → Methanol, Uremia (renal failure), DKA, Phenformin (weird drug you don't need to worry about), Iron tablets / Isoniazid, Lactic acidosis, Ethylene glycol (antifreeze), Salicylates (aspirin). - If the patient has metabolic acidosis and the anion gap is normal in the Q, you can eliminate the MUDPILES answers and choose an answer like renal tubular acidosis (RTA). - Anion gap is calculated as $\text{Na}^+ - (\text{HCO}_3^- + \text{Cl}^-)$. - Anion gap of 8-12 is normal. So 13 or greater is high. I specifically write “13 or greater” because there is an NBME Q where anion gap comes out to 12, and they want renal tubular acidosis. I talk in detail in the HY Renal PDF about RTA.
Normal anion-gap metabolic acidoses	- Diarrhea, RTA, adrenal insufficiency, and CAH (21-deficiency) are most important.
Metabolic alkalosis	<ul style="list-style-type: none"> - High pH caused by high HCO₃⁻; pCO₂ will go up to compensate. - Conn syndrome, renal artery stenosis, fibromuscular dysplasia, vomiting, loops and thiazides (promote RAS activation due to volume depletion).
Respiratory acidosis	<ul style="list-style-type: none"> - Low pH caused by high CO₂; HCO₃⁻ goes up <i>if chronic</i> to compensate (bicarb is basic). - Acute (normal bicarb): hypoventilation due to opioids, benzos, barbiturates. - Chronic (high bicarb): COPD, obstructive sleep apnea, obesity, ankylosing spondylitis, severe kyphoscoliosis.
Respiratory alkalosis	<ul style="list-style-type: none"> - High pH caused by low CO₂; HCO₃⁻ goes down <i>if chronic</i> to compensate. - Acute (normal bicarb): asthma attack, panic attack, most pulmonary emboli, altitude sickness (first day at high altitude). - Chronic (low bicarb): living at high altitude, pregnancy (progesterone upregulates respiratory center).
<ul style="list-style-type: none"> - Should be noted that primary metabolic acid/base derangements are compensated for instantly by changes in respiration (i.e., it's easy to retain or breathe off CO₂ merely by changing respiratory rate), whereas primary respiratory derangements are compensated for slowly because it takes time for the kidney to alter bicarb excretion. - Winter formula is used to calculate predicted pCO₂ based on any change in bicarb, where: Predicted pCO₂ = $(1.5 \times \text{HCO}_3^-) + 8 \pm 2$. For example, if a patient has DKA and bicarb is 14 mEq/L, we expect pCO₂ to be 27-31 mmHg. If pCO₂ is lower than 27, then the patient has a concurrent respiratory alkalosis; if higher than 31, then the patient has a concurrent respiratory acidosis. 	

Salicylate toxicity

- Diagnosis is salicylate (aspirin) toxicity. Tinnitus (ear-ringing) is the most common first symptom.
- This patient has mixed metabolic acidosis-respiratory alkalosis (i.e., both a metabolic acidosis and respiratory alkalosis at the same time).
- Aspirin initially causes an isolated respiratory alkalosis (within the first 20 minutes) due to direct upregulation of respiratory centers in the brain.
- However, aspirin itself is an acid (salicylic acid), so it will ultimately cause a metabolic acidosis that wins over the respiratory alkalosis (i.e., pH will ultimately go low).
- Anion gap is high. Salicylates are the S in MUDPILES.
- Sodium and potassium are normal in salicylate toxicity. I have seen these arrows listed before, which causes students confusion, but they are unchanged. Sometimes the Q will give you numerical values where you need to calculate anion gap – i.e., $\text{Na}^+ - (\text{HCO}_3^- + \text{Cl}^-)$. The value must be 13 or greater since it is one of the MUDPILES. Normal range is 8-12.
- In summary, once again, for aspirin:
 - First 20 mins: acute respiratory alkalosis ($\uparrow \text{pH}$, $\leftrightarrow \text{HCO}_3^-$, $\downarrow \text{CO}_2$).
 - After 20 mins: mixed metabolic acidosis-respiratory alkalosis ($\downarrow \text{pH}$, $\downarrow \text{HCO}_3^-$, $\downarrow \text{CO}_2$, \uparrow anion-gap).
- The low bicarbonate we see after 20 minutes **is not compensation**. It coincidentally goes low (as we'd expect for renal compensation in the setting of respiratory alkalosis). But remember that the kidney cannot induce this change until a minimum of 12-24 hours later. The reason bicarb is low after 20 minutes is because aspirin itself is an acid that is causing a metabolic acidosis and driving the bicarb low.
- A 2CK-level point is that Na^+ and Cl^- can be abnormal insofar as the bicarb is low and anion gap is high.
- Potassium must always be normal.
- You might get an aspirin Q where you're forced to choose either an up or down arrow for chloride and you say, "I haven't heard of that before. I thought it would just be normal." But if you're forced to choose, clearly you'd go with the answer where chloride is low, since anion gap is calculated as $\text{Na}^+ - (\text{HCO}_3^- + \text{Cl}^-)$, and a low chloride would make the anion gap higher than the answer choice with high chloride.

Renal failure key disturbances

- As discussed earlier, renal failure causes secondary hyperparathyroidism, where we have:
 - $\downarrow \text{Ca}^{2+}$, $\uparrow \text{PO}_4^{3-}$, $\uparrow \text{PTH}$, $\downarrow 1,25\text{-D}_3$.
- However, it is also pass-level you know that in renal failure we also have:
 - $\uparrow \text{K}^+$, $\downarrow \text{HCO}_3^-$, $\downarrow \text{pH}$, \uparrow anion gap (U in MUDPILES = uremia = renal failure), with Na^+ variable.
 - The kidney normally secretes potassium distally in the cortical collecting duct under the action of aldosterone. So if the kidney is fucked up, we can't do that, so K^+ is \uparrow .
 - Likewise, we normally have HCO_3^- reabsorbed in the PCT and H^+ secreted in the cortical collecting duct, so if we can't do either of those things, blood HCO_3^- and pH \downarrow .

HY Pulmonary acid/base findings

- Acute asthma attack and PE: $\downarrow \text{pCO}_2$, no change HCO_3^- , $\uparrow \text{pH}$,
 - The key here is that these conditions cause acute respiratory alkalosis, not acidosis, as I mentioned in above table. Students normally fuck this up and think pCO_2 is high. pCO_2 only goes \uparrow if the patient becomes tired as an asthma attack prolongs. But initially, for both of these conditions, we have low pCO_2 (holy shit), not high. Bicarb is unchanged because it takes a minimum of 12-24 hours for bicarb excretion to be sufficiently modulated by the kidney.
 - Tangentially, metabolic acid-base disturbances are instantly compensated for by changes in pCO_2 by simply breathing more or less.
- Patients with COPD and obstructive sleep apnea are **chronic CO_2 retainers**, where we have:
 - $\uparrow \text{pCO}_2$, $\uparrow \text{HCO}_3^-$, $\downarrow \text{pH}$.
 - Bicarb goes up to compensate.

Miscellaneous HY acid/base	
Vomiting	<ul style="list-style-type: none"> - ↓ Serum K⁺, ↓ Cl⁻, ↑ HCO₃⁻, ↑ CO₂, ↑ pH. - Very high-yield you know that vomiting causes a hypokalemic, hypochloremic, metabolic alkalosis. - Vomitus contains lots of potassium, chloride, and protons. In addition, volume depletion can promote distal renal losses of K⁺ and H⁺ secondary to RAAS upregulation. - CO₂ is acidic, so we want to retain it to compensate.
Loop/thiazide diuretic abuse	<ul style="list-style-type: none"> - ↓ Serum K⁺, ↓ Cl⁻, ↑ HCO₃⁻, ↑ CO₂, ↑ pH. - Furosemide is a loop diuretic. It will block the apical 2Cl⁻/K⁺/Na⁺ symporter in the thick ascending limb. Since water follows ions, and ion reabsorption is impaired, increased diuresis (urination) occurs. Volume loss causes upregulation of RAAS and distal secretion of protons under the control of aldosterone, leading to metabolic alkalosis. This is referred to as “contraction alkalosis,” where volume contraction induced by diuretics promotes metabolic alkalosis. In addition, additional distal secretion of K⁺ occurs. - Thiazide diuretics will also follow this arrow pattern. They block the Na⁺/Cl⁻ symporter on the apical membrane of the early-DCT, leading to volume depletion and ↑ RAAS, thereby ↑ H⁺ and K⁺ secretion distally. - CO₂ is acidic and retained because it compensates for our metabolic alkalosis. - It should be noted that these arrows are the same as for vomiting.
Diarrhea	<ul style="list-style-type: none"> - ↓ Serum K⁺, ↑ Cl⁻, ↓ HCO₃⁻, ↓ pH, ↓ CO₂, ↔ anion gap. - Stool is rich in potassium and bicarb. Diarrhea and laxative abuse can cause a normal anion-gap metabolic acidosis. Since CO₂ is acidic, we blow this off to compensate. - Serum chloride is high due to cellular shifts. - Anion gap is normal because diarrhea is not part of MUDPILES.
Laxative abuse	<ul style="list-style-type: none"> - ↓ Serum K⁺, ↑ Cl⁻, ↓ HCO₃⁻, ↓ CO₂, ↓ pH, ↔ anion gap. - Stool is rich in potassium and bicarb. Diarrhea and laxative abuse can cause a normal anion-gap metabolic acidosis. Since CO₂ is acidic, we blow this off to compensate. - Serum chloride is high due to cellular shifts.

Endocrine pharm for IM (keeping things HY)	
Metformin	<ul style="list-style-type: none"> - MOA = “↑ Glycolysis + ↓ gluconeogenesis.” - Only used for type II DM. - Causes lactic acidosis. - Discontinue if bicarb is low (means lactic acidosis). - Discontinue (or don’t commence) if creatinine is 1.5 or greater, as reduced renal function ↑ risk of lactic acidosis. - Choose insulin over metformin for regulation of glycemic control in pregnancy / intrapartum, as it allows for optimal fine-tuning / control of glucose. - USMLE can give you patient on metformin who had CT with contrast + gets high creatinine as a result + they ask you what would have prevented the increase in creatinine prior to the CT → answer = “infusion of 0.9% saline” or “adequate intravenous hydration”; the wrong answer is “discontinuation of metformin.” This one is a little tricky, where you need to know that adequate hydration saline hydration is the #1 way to prevent contrast nephropathy. There is ↑ risk of lactic acidosis due to metformin in patients who have renal insufficiency, but metformin itself doesn’t cause renal insufficiency. In other words, ↑ creatinine is a reason to stop metformin, but ↑ creatinine doesn’t result from metformin itself.
Insulin	<ul style="list-style-type: none"> - USMLE doesn’t give a fuck that you know about all of the different insulin types and their durations of action. - What USMLE might do on 2CK is give you a patient with diabetes who wakes up with severe hyperglycemia + ask you what needs to be done. The answer = decrease, not increase (holy shit), dose of evening intermediate-acting insulin. This is called Somogyi phenomenon, where it appears as though because morning glucose is elevated, this means evening/night insulin is insufficient. But it’s actually

	<p>the opposite, where the evening/night dose is too high, which pushes the patient into overnight hypoglycemia, causing a compensatory sympathetic response that results in a robust rebound hyperglycemia by morning.</p> <p>- The other Q they will give is a patient with type II DM who is already on metformin + glyburide who has uncontrolled HbA1c at 12% + give you either low bicarb or high creatinine → they ask what needs to be done → answer = “discontinue metformin and glyburide and commence intermediate-acting insulin.” I’ve made YouTube clips on this Q and have talked about it many times, as it gets asked in our Telegram group probably once a month. The point is that 1) if a patient has low bicarb while on metformin, this means lactic acidosis due to metformin, so you must choose an answer choice where metformin is discontinued; and 2) a patient who has a creatinine of 1.5 or greater needs to be off metformin (I’ve seen max 1.4 on NBME where metformin is acceptable), since renal insufficiency is a risk factor for lactic acidosis due to metformin.</p>
Sulfonylureas	<p>- Glyburide, glipizide, glibenclamide.</p> <p>- Insulin secretagogues – i.e., ↑ insulin secretion by blocking the ATP-gated K⁺ channel on β-islet cells without the need for ATP.</p> <p>- Glyburide and glipizide tend to be the ones that shows up repeatedly on NBME. I don’t think I’ve ever seen other sulfonylurea on NBME for that matter.</p> <p>- Glibenclamide was known for causing severe hypoglycemia. You could be aware of this in theory.</p>
Meglitinides	<p>- Repaglinide.</p> <p>- Similar to sulfonylureas, these ↑ insulin secretion by blocking the ATP-gated K⁺ channel on β-islet cells without the need for ATP.</p>
GLP-1 analogues	<p>- Liraglutide, semaglutide (Ozempic).</p> <p>- Glucagon-like peptide-1 stimulates insulin release.</p>
DPP-4 inhibitors	<p>- Sitagliptin.</p> <p>- DPP-4 is an enzyme that breaks down GLP-1, so if we inhibit DPP-4, GLP-1 is ↑.</p> <p>- Therefore, ↑ insulin release from the pancreas.</p>
Thiazolidinediones	<p>- Pioglitazone.</p> <p>- ↑ insulin sensitivity at tissues by stimulating PPAR-γ.</p> <p>- Can cause liver toxicity.</p>
α-glucosidase inhibitors	<p>- Acarbose, miglitol</p> <p>- ↓ Glucose absorption in small bowel.</p> <p>- Can cause diarrhea.</p>
SGLT-2 inhibitors	<p>- Dapagliflozin.</p> <p>- ↓ Glucose reabsorption in the PCT of the kidney.</p> <p>- Can ↑ risk of candidal infections.</p>
Amylin analogues	<p>- Pramlintide.</p> <p>- Amylin is a hormone that is co-secreted with insulin from β-cells that suppresses glucagon secretion, slows gastric emptying, and promotes satiety, thereby preventing a rapid increase in postprandial blood glucose.</p>
PTU/methimazole	<p>- Propylthiouracil (PTU) and methimazole are both used for Graves.</p> <p>- Both inhibit thyroperoxidase; PTU has an additional MOA of inhibiting 5-deiodonise.</p> <p>- Both PTU and methimazole can cause neutropenia/agranulocytosis. You need to know this often presents as mouth ulcers on USMLE. For example, they’ll say patient was recently treated in hospital for thyroid storm + now has mouth ulcers and fever → answer = “drug adverse effect,” or “drug-induced neutropenia.”</p> <p>- Propranolol is used for tachycardia in hyperthyroidism (beta-blockade inhibits 5-deiodonase). Steroids are used for exophthalmos.</p> <p>- Methimazole is teratogenic in first-trimester.</p>
Demeclocycline	<p>- Shows up as Tx for SIADH on NBME.</p> <p>- Tetracycline antibiotic that causes nephrogenic DI as an adverse effect, but this is actually a “good thing” if we want to treat SIADH (i.e., let’s just treat one problem by causing another problem, and they somehow cancel out).</p>

Desmopressin	<ul style="list-style-type: none">- Vasopressin (ADH) analogue used as treatment for central DI.- Also used after fluid restriction in DI cases for differentiating central from nephrogenic.
Octreotide	<ul style="list-style-type: none">- Somatostatin analogue used for acromegaly and esophageal varices.
Cinacalcet	<ul style="list-style-type: none">- Increases sensitivity of calcium-sensing receptors on parathyroid glands.- Helps to suppress PTH in secondary hyperparathyroidism.

IM mixed bullet points

- Travel + self-limiting watery or brown/green diarrhea → Traveler diarrhea = ETEC HL or HS toxin
- Bloody diarrhea + poultry consumption → Campylobacter jejuni or Salmonella spp.
- Abx (clindamycin, beta-lactam, cephalosporin) + diarrhea → C. difficile
- Dx of C. diff → stool AB toxin test, **not** stool culture
- Fever of 104 + abdo distension in C diff → toxic megacolon → laparotomy
- Tx of C. diff → **vancomycin, not metronidazole (updated guidelines as of Feb 2018)**
- Bloody diarrhea + travel → Entamoeba histolytica
- Tx of E. histolytica → metronidazole + iodoquinol; can give paromomycin
- Close quarters or military barracks or cruise ship + watery diarrhea → Norwalk virus
- Child <5 years + watery diarrhea → rotavirus
- Few organisms causing bloody diarrhea → Shigella
- Bloody diarrhea + appendicitis-like pain (pseudoappendicitis) in a child → Yersinia enterocolitica
- Bloody diarrhea + reactive arthritis in an adult → Y. enterocolitica, Campylobacter, Shigella, Salmonella
- Diarrhea + Guillain-Barre syndrome → Campylobacter
- GBSyndrome CSF? → albuminocytologic dissociation (high protein + normal cells)
- GBSyndrome Dx? → electromyography + nerve conduction studies (on NBME)
- Cardiac ischemia + need to evaluate → ECG stress test first-line
- Cardiac ischemia + abnormal baseline ECG (e.g., BBB) → Echo stress test (need normal ECG to do ECG stress test)
- Cardiac ischemia + patient can't exercise → dobutamine + ECG/echo
- ECG shows diffuse ST-segment elevations → pericarditis
- Pericarditis Tx → NSAID, or steroid, or colchicine
- Central chest pain worse when supine; better when leaning forward → pericarditis
- Lateral chest pain after viral infection + increased CK → pleurodynia (intercostal muscle spasm)
- ST-segment depressions in the anterior ECG leads → posterior MI
- Electrical alternans on ECG → pericardial tamponade / pericardial effusion

- Pulsus paradoxus (drop in systolic BP >10 mm with inspiration) → cardiac tamponade or severe asthma
- Beck triad → hypotension + muffled heart sounds + JVD → pericardial tamponade
- Tx of tamponade → pericardiocentesis or pericardial window
- Tamponade → do echo before pericardiocentesis if both listed (even though sounds wrong, on 2CK NBME)
- Community-acquired pneumonia (CPP) + bilateral CXR infiltrates → Mycoplasma
- CPP + lobar pattern (right-lower lobe consolidation + dullness to percussion) → Strep pneumo
- CPP + lobar pattern, but they say “interstitial” in the vignette description → Mycoplasma, not S. pneumo
- Empiric Tx for CPP → azithromycin
- Tx for CPP is pt on Abx past three months → fluoroquinolone over azithro
- Pneumonia in CF patient <10 years → S. aureus exceeds Pseudomonas
- Pneumonia in CF patient >10 years → Pseudomonas exceeds S. aureus.
- Pneumonia after influenza infection → USMLE wants S. aureus
- Pneumonia + rabbits → F. tularensis
- Pneumonia + cattle → Coxiella (Q fever)
- Pneumonia + birds → Chlamydia psittaci
- Leg swelling + pain + shortness of breath → Pulmonary embolism caused by DVT
- Tx of PE → Heparin before spiral CT
- Tx of PE in pregnant woman → V/Q scan, not CT
- Tx of PE in someone already on warfarin → spiral CT to confirm, then IVC filter
- Acid-base disturbance in PE → resp. alkalosis (low CO₂, high pH, low O₂, normal bicarb [too acute to change])
- Acid-base disturbance in asthma → resp. alkalosis (low CO₂, high pH, low O₂, normal bicarb [too acute to change])
- Acid-base disturbance in aspirin toxicity first 20 mins → resp. alkalosis (low CO₂, high pH, normal O₂, normal bicarb [too acute to change])

- Acid-base disturbance in aspirin toxicity after 20 mins → mixed metabolic acidosis-respiratory alkalosis (low CO₂, low pH, normal O₂, low bicarb)
- Tx for aspirin toxicity → bicarb (increased excretion through urinary alkalization)
- Tx for TCA toxicity → sodium bicarb → dissociates drug from myocardial sodium channels
- Normal calcium → 8.4-10.2 mEq/L
- Tx of hypercalcemia → 10.2-12 → normal saline (0.9% NaCl)
- Tx of hypercalcemia → 12-14 → normal saline (0.9% NaCl) only if asymptomatic; add bisphosphonate (e.g., pamidronate) if symptomatic
- Tx of hypercalcemia → 14+ → normal saline (0.9% NaCl) + bisphosphonate
- High calcium + polyuria → nephrogenic diabetes insipidus (weird, but on NBME)
- High calcium + confusion → delirium caused by high calcium
- Low calcium or potassium not responsive to supplementation → cause is low Mg
- Low calcium or potassium in alcoholic → hypomagnesemia is cause
- Ataxia, confusion, ophthalmoplegia → Wernicke encephalopathy (B1 deficiency)
- Retrograde amnesia + confabulation in alcoholic → Korsakoff psychosis
- Wernicke-Korsakoff syndrome → mammillary bodies
- Hx of many pregnancies + downward movement of vesicourethral junction → stress incontinence
- Tx of stress incontinence → pelvic floor exercises (Kegel); if insufficient → mid-urethral sling
- Hyperactive detrusor or detrusor instability → urge incontinence
- Need to run to bathroom when sticking key in a door → urge incontinence
- Incontinence in multiple sclerosis patient or perimenopausal → urge incontinence
- Tx of urge incontinence → oxybutynin (muscarinic cholinergic antagonist) or mirabegron (beta-3 agonist)
- Incontinence + high post-void volume (usually 3-400 in question; normal is <50 mL) → overflow incontinence
- Incontinence in diabetes → overflow incontinence due to neurogenic bladder
- Tx for overflow incontinence in diabetes → bethanacol (muscarinic cholinergic agonist)
- Incontinence in BPH → overflow incontinence due to outlet obstruction → eventual neurogenic bladder

- Tx for overflow incontinence in BPH → insert catheter first; then give alpha-1 blocker of 5-alpha-reductase inhibitor; then TURP if necessary
- Exquisitely tender prostate on digital rectal exam → prostatitis
- Prostatitis Tx → ciprofloxacin (fluoroquinolone → DNA gyrase / topoisomerase II inhibitor)
- Costovertebral angle tenderness + fever → pyelonephritis
- Costovertebral angle tenderness + granular casts → pyelonephritis (correct, super-weird; NOT acute tubular necrosis; this is on 2CK NBME)
- Tx for pyelonephritis → ciprofloxacin, OR ampicillin + gentamicin
- Saddle anesthesia + urinary retention → cauda equina syndrome
- Perianal anesthesia + urinary retention or incontinence → conus medullaris syndrome
- Gradual-onset dementia + no sensory or motor dysfunction → Alzheimer
- Mini-mental state exam score low + patient tries to do well → Alzheimer
- Mini-mental state exam score low + patient is apathetic / takes long to perform tasks / does poorly on reverse serial 7s → depression (pseudodementia)
- Patient complains about memory loss → normal aging, not Alzheimer
- First-line Tx for Alzheimer → donepezil (cholinesterase inhibitor → increases cholinergic transmission); can also give galantamine or rivastigmine
- NMDA receptor (glutamate receptor) antagonist used in Alzheimer Tx → memantine
- Step-wise dementia/decline and/or sensory/motor disturbance → vascular dementia
- Hx of hypertension + dementia + sensory/motor disturbance → vascular dementia
- Visual hallucinations + Parkinsonism + dementia → Lewy body dementia
- Apathy + disinhibition + personality change + dementia → frontotemporal dementia (Pick disease)
- Urinary incontinence + ataxia + CNS dysfunction (wet, wobbly, wacky) → Normal-pressure hydrocephalus
- Wet, wobbly, wacky + Parkinsonism → still NPH
- Parkinsonism in young patient → Wilson disease till proven otherwise
- Parkinsonism in older patient → Parkinson disease
- Parkinsonism + axial dystonia → progressive supranuclear palsy
- Tx of UTI → TMP/SMX or nitrofurantoin

- Tx of cystitis → nitrofurantoin (need not be pregnant)
- Waiter tip position in kid → upper brachial plexus injury → C5/6 → Erb-Duchenne palsy
- Claw hand → lower brachial plexus → C8/T1 → Klumpke palsy
- Pronated arm + wrist-drop → radial nerve injury
- Midshaft fracture of humerus → Radial nerve injury
- Supracondylar fracture of humerus → median nerve injury
- Surgical neck of humerus fracture → axillary nerve injury
- Medial epicondylar injury → ulnar nerve injury
- Weakened biceps + loss of sensation of lateral forearm → musculocutaneous nerve injury
- Paresthesias + pain following burn or casting → compartment syndrome
- Compartment syndrome Dx → measure compartment pressure
- Compartment syndrome Tx → fasciotomy of uncast
- Guy lifts heavy box → severe lower back pain + muscle spasm + no radiculopathy → lumbosacral strain only
- Lumbosacral strain diagnosis → DO NOT x-ray
- Lumbosacral strain Tx → NSAIDs + exercise as tolerated; bedrest is the WRONG answer
- Guy lifts heavy box → severe lower back pain + radiculopathy → herniated disc; yes, x-ray.
- Point tenderness over a vertebra in older woman → osteoporosis (compression fracture)
- Point tenderness over a vertebra in younger patient on steroids → osteoporosis (compression fracture)
- Point tenderness over a vertebra in patient with autoimmune disease → recognize patient is on steroids → osteoporosis (compression fracture)
- Point tenderness over a vertebra in IV drug user → epidural abscess
- "Step-off" of one vertebra relative to another → spondylolisthesis
- Back pain worse in the morning and gets better throughout day in male 20s-40s → ankylosing spondylitis
- Bamboo spine → ankylosing spondylitis
- Dx of AS → x-ray of sacroiliac joints
- Back pain worse when standing or walking for long periods of time → lumbar spinal stenosis

- Radiculopathy down an arm → cervical disc herniation
- Bilateral paresthesias in the arms in rheumatoid arthritis patient → atlantoaxial subluxation
- Bilateral paresthesias in the arms in rheumatoid arthritis patient → MR of spine to Dx atlantoaxial subluxation
- Prior to surgery in rheumatoid arthritis patient → cervical CT or flexion/extension x-rays of cervical spine to check for atlantoaxial subluxation
- Back pain in elderly patient with hypercalcemia → multiple myeloma or metastases
- Back in pain in patient with history of other type of cancer → metastases
- Suspected spinal mets → MRI
- Metastases to long bones in prostate cancer → osteoblastic (Dx with bone scan); spine do MRI
- High hemoglobin +/- pruritis after shower +/- plethora +/- splenomegaly → polycythemia vera
- High hemoglobin + low EPO → polycythemia vera
- Pruritis after shower → basophilia
- High hemoglobin + lung disease / low pO₂ → secondary polycythemia (high EPO)
- Polycythemia + hypercalcemia + smoker + red urine → RCC (paraneoplastic EPO + PTH-rp)
- Blurry vision or Raynaud or pain in fingers or headache → hyperviscosity syndrome
- Hyperviscosity syndrome → Waldenstrom macroglobulinemia or polycythemia
- Hereditary spherocytosis → AD, ankyrin or spectrin or band protein deficiency; Tx = splenectomy
- Treatment for ITP → steroids, then IVIG, then splenectomy
- Tx for hereditary hemochromatosis → serial phlebotomy
- Tx for secondary hemochromatosis (transfusional siderosis) → chelation therapy (deferrioxamine)
- Viral infection + tinnitus + vertigo +/- neurosensory hearing loss → labyrinthitis
- Viral infection + vertigo → vestibular neuritis
- Tx for multiple sclerosis flares → IV steroids (IV methylprednisolone)
- Given to MS patients between flares → interferon-beta
- Tx for spasticity in MS → baclofen (GABA-B receptor agonist)
- Incontinence in MS → urge (hyperactive detrusor, as mentioned earlier)
- New-onset murmur + fever → endocarditis till proven otherwise
- Empiric Tx for endocarditis → vancomycin or ampicillin/sulbactam, PLUS gentamicin

- Beta-lactam (e.g., nafcillin) or cephalosporin + rash + renal issue → interstitial nephritis
- Interstitial nephritis → WBCs in the urine (eosinophils)
- Fixed splitting of S2 → atrial septal defect
- Holosystolic murmur at left sternal border PLUS either parasternal heave or palpable thrill → VSD
- Holosystolic murmur at left sternal border PLUS diastolic rumble → also VSD
- To-and-fro murmur → PDA (on 2CK NBME)
- Pan-systolic-pan-diastolic murmur → PDA
- Continuous, machinery-like murmur → PDA
- Congenital rubella syndrome → PDA
- Heart problem in neonate of mom with SLE → congenital third-degree heartblock
- Heart problem in William syndrome → supraaortic stenosis
- Bicuspid aortic valve → aortic stenosis
- Mid-systolic (crescendo-decrescendo) murmur + gets worse with Valsalva → HOCM
- Mid-systolic (crescendo-decrescendo) murmur + no change or softens with Valsalva → aortic stenosis
- Myxomatous degeneration of mitral valve → mitral valve prolapse
- Marfan or Ehlers-Danlos syndrome → MVP or aortic regurg
- Rheumatic heart disease acutely (onset of Group A Strep infection) → mitral regurg
- Rheumatic heart disease later on (years after infection) → mitral stenosis
- Mid-systolic click → MVP
- Late-peaking systolic murmur with ejection click → another way they describe aortic stenosis
- Bounding pulses + massively wide pulse pressure → aortic regurg
- Brisk upstroke + precipitous downstroke of pulse → aortic regurg
- Syncope + angina + dyspnea (SAD) → aortic stenosis
- Dyspnea in second trimester of pregnancy → mitral stenosis
- Dyspnea late in pregnancy → peripartum cardiomyopathy
- Screening at age 50 → mammogram (every two years) + colonoscopy (every ten years)
- Colon cancer in first-degree relative (sibling or parent) → start at age 40 or ten years before diagnosis in relative, whichever is earlier, and do every 5 years.

- Breast imaging (if performed) → ultrasound only under age 30; over age 30 do mammogram +/- ultrasound
- Anuria (no urine output) after removal of catheter → acute urethral obstruction
- Contrast induced nephropathy; how to prevent → saline hydration beforehand
- BUN/Cr > 20 → prerenal (hypovolemia) → heart failure
- BUN/Cr < 20 → not prerenal (15-20 for post-renal, and <15 for intra-renal is wrong on 2CK NBMEs)
- Blood loss + oliguria → acute tubular necrosis
- Blood loss + obstetric catastrophe → diffuse cortical necrosis
- Sickle cell + nephrotic syndrome → focal segmental glomerulosclerosis
- Sickle cell + red urine → renal papillary necrosis
- 2+ blood in urine but 0-4 RBCs/HPF on LM → false + blood on dipstick → myoglobinuria → rhabdomyolysis
- Pleural / supradiaphragmatic plaques → asbestosis
- Preferred antibiotic in sepsis → ceftriaxone
- Sepsis Tx in young children → cefotaxime
- Tx for spontaneous bacterial peritonitis → ceftriaxone
- Cirrhosis or recent peritoneal dialysis or nephrotic syndrome + fever + abdo pain → SBP
- SBP Dx → paracentesis (peritoneal aspiration; don't confuse with pericardiocentesis) + do gram-stain + look for >250 WBCs per HPF
- Dysphagia to solids and liquids at the same time to start → says neurogenic cause → achalasia
- Dysphagia to solids that **progresses** to solids and liquids → esophageal cancer
- Halitosis +/- gurgling sound when swallowing +/- regurgitation of undigested food → Zenker
- Zenker + achalasia initial Dx modality → barium swallow
- After barium swallow is done and shows bird's beak appearance → manometry to confirm Dx of achalasia
- Pt with Hx of GERD + dysphagia → straight to endoscopy to rule out cancer
- Diabetic pt with new-onset GERD → diabetic gastroparesis
- Diabetic pt with new-onset GERD → give metoclopramide, not PPI
- Diabetic gastroparesis before giving med → endoscopy first to rule out physical obstruction

- Endoscopy negative for diabetic gastroparesis → do gastric-emptying scintigraphy
- Bulimia nervosa or anorexia → never give bupropion (seizure risk)
- Electrolyte abnormality in anorexia → hypokalemia
- Most common cause of death in anorexia → arrhythmia from hypokalemia
- Refeeding syndrome → worry about hypophosphatemia
- Tx of anorexia + depression → mirtazapine (alpha-2 antagonist); stimulates appetite
- Amenorrhea in anorexia → low FSH + low estrogen (hypogonadotropic)
- Premature ovarian failure + Turner syndrome + menopause → high FSH (low inhibin) + low estrogen
- Cholelithiasis → Dx with abdo ultrasound; fat, forties, female, fertile
- Biliary colic + fever → cholecystitis
- Tx of cholelithiasis + cholecystitis → cholecystectomy
- Pt doesn't want surgery or is pregnant → ursodeoxycholic acid (ursodiol)
- Abdo USS negative in suspected cholecystitis → HIDA scan
- Gall bladder doesn't light up on HIDA scan → confirms cholecystitis
- Cholelithiasis in pregnancy → estrogen upregulates HMG-CoA reductase + progesterone slows biliary peristalsis
- Trichotillomania (eating one's hair) + GI symptoms → gastric bezoar (hair ball)
- Hx of surgery + high-pitched bowel sounds or acute-onset abdo symptoms → small bowel obstruction (SBO)
- Renal failure + friction rub over chest → uremic pericarditis → do hemodialysis
- High leukocytes + high leukocyte ALP → leukemoid reaction
- High leukocytes + low leukocyte ALP → CML
- Metamyelocytes + myelocytes + splenomegaly → CML
- Tx of CML → imatinib; causes fluid retention / edema
- Smudge cells + autoimmune hemolytic anemia → CLL
- Auer rods → AML; composed of myeloperoxidase
- Tx of AML → DIC caused by Auer rod release into blood
- Kid with high lymphocytes → ALL or pertussis (weird bc bacterial, but lymphocytes often >30k)
- Dry cough in winter → cough-variant asthma (1/3 of asthmatics only have cough)

- Young African American woman + dry cough + normal CXR → asthma (activation of mast cells), not sarcoidosis
- Young African American woman + dry cough + nodularity on CXR → sarcoidosis (noncaseating granulomas)
- Electrolyte disturbance in sarcoid → hypercalcemia → LOW PTH + high calcium
- Hypercalcemia in sarcoid, why? → epithelioid (activated) macrophages produce 1-alpha hydroxylase, thereby activating vitamin D3
- Increased calcium in sarcoid → means decreased calcium in feces (bc D3 increased small bowel absorption)
- Tx for sarcoid → steroids
- Outpatient Tx of asthma → SABA, then low-dose ICS, then maximize dose of ICS, then LABA, then use any number of drugs (e.g., mast cell stabilizers, anti-leukotriene, etc.), then oral steroids last resort
- Kid with asthma on SABA inhaler + not effective + next best step? → ICS (fluticasone)
- Kid with asthma on SABA inhaler + most effective way to decrease recurrence? → oral steroids (not next best step, but certainly most effective)
- 40s male + hematuria + hemoptysis → Goodpasture syndrome
- Antibodies in Goodpasture → Anti-GBM (anti-collagen IV)
- Dx of Goodpasture → antibodies first, but confirmatory is renal biopsy showing linear immunofluorescence
- Hematuria + hemoptysis + “head-itis” (mastoiditis, sinusitis, otitis, nasal septal perforation) → Wegener
- New name for Wegener → granulomatosis with polyangiitis
- Dx of Wegener → c-ANCA (anti-PR3; anti-proteinase 3)
- Asthma + eosinophilia → Churg-Strauss
- New name for CS → eosinophilic granulomatosis with polyangiitis
- Dx of CS → p-ANCA (anti-MPO; anti-myeloperoxidase)
- Hematuria in isolation + p-ANCA in serum → microscopic polyangiitis (MP)
- Severe renal disease in Wegener or Goodpasture or MP → rapidly progressive glomerulonephritis (crescentic)

- High ALP + high direct bilirubin + high amylase or lipase → gallstone pancreatitis = choledocholithiasis
- High ALP + high direct bilirubin + high amylase or lipase + remote Hx of cholecystectomy → sphincter of Oddi dysfunction (can't be a stone cuz the gallbladder was removed ages ago)
- High ALP + high direct bilirubin + normal amylase or lipase in someone with recent cholecystectomy → choledocholithiasis (retained stone in cystic duct that descended, but not distal to pancreatic duct entry point)
- Dx and Tx of choledocholithiasis → ERCP
- High ALP + high direct bilirubin + normal amylase or lipase in someone with remote cholecystectomy → pancreatic cancer
- Dx of pancreatic cancer → CT abdo with contrast
- High ALP + high direct bilirubin + normal amylase or lipase in someone with remote cholecystectomy + CT is negative → cholangiocarcinoma
- High ALP + high direct bilirubin + normal amylase or lipase + diffuse pruritis + high cholesterol → primary biliary cirrhosis (PBC)
- High ALP + high direct bilirubin + normal amylase or lipase + autoimmune disease (in pt or family) → PBC
- Dx of PBC → anti-mitochondrial Abx next best step; liver biopsy is confirmatory
- Recent cholecystectomy + fever + abdo pain → post-op bile leak
- High ALP + high direct bilirubin + normal amylase or lipase + CT shows cystic lesion in bile duct → choledochal cyst → do simple excision of cyst (cholangiocarcinoma not cystic + CT can be negative)
- Imaging to view liver or pancreas → CT with contrast
- Imaging to view gallbladder → Ultrasound
- Imaging to view gallbladder in suspected cholecystitis only if USS negative → HIDA scan
- Imaging to view bile ducts → ERCP or MRCP (choose ERCP > MRCP if both listed)
- Teenage girl with Hx of cutaneous candida infections since childhood → chronic mucocutaneous candidiasis
- MCC → answer = T cell dysfunction = impaired cell-mediated immunity on the USMLE
- Bacterial + fungal + protozoal + viral infections since birth → SCID
- Bacterial infections since age 6 months → Bruton

- Bacterial infections only since birth → Bruton (rare as hell to say from birth, but it's on new 2CK NBME)
- SCID XR variant → common gamma-chain mutation (IL-2 receptor deficiency)
- SCID AR variant → adenosine deaminase deficiency
- Bruton mechanism → tyrosine kinase mutation
- Hyper IgM syndrome → deficiency of CD40 ligand on T cell (can't activate CD40 on B cell to induce isotype class switching)
- Greasy, scaly scalp + itchy + papules + adult → seborrheic dermatitis
- Tx for SD → azole or selenium shampoo
- Tx for tinea capitis → oral griseofulvin for patient only
- How to decrease risk of tinea capitis → avoidance of sharing of hats
- Tx of onychomycosis (nailbed fungus) → oral terbinafine
- Tx of tinea pedis → topical terbinafine or topical azole
- Tx of tinea corporis (ring worm) → topical azole (clotrimazole or miconazole)
- Tx of cutaneous candida → oral azole
- Tx of oropharyngeal candida → nystatin mouthwash
- Tx of esophageal candidiasis → oral azole, not nystatin mouthwash
- Tx of vaginal candidiasis → topical nystatin before trying oral azole
- Odynophagia (painful swallowing) in immunocompromised pt → esophageal candidiasis till proven otherwise
- CNS fungal infection or fungemia (rigors/chills) → amphotericin B
- Cryptococcal meningitis → amphotericin B + flucytosine, then do fluconazole taper
- Simple fungal pneumonia → fluconazole
- Sporothrix schenckii (rose thorn + finger papule) → itraconazole
- Hypopigmentation on upper back / trunk → tinea versicolor (Malassezia furfur)
- Tx of tinea versicolor → topical selenium
- Most common cause of impetigo → S. aureus now exceeds S. pyogenes
- Tx of impetigo → topical mupirocin
- Beefy red, well-demarcated skin plaque → erysipelas

- Most common cause of erysipelas → Group A Strep (*S. pyogenes*) >>> *S. aureus*
- More diffuse pink skin lesion + tenderness + fever → cellulitis
- Most common cause of cellulitis → *S. aureus* exceeds *S. pyogenes*
- Tx of erysipelas + cellulitis → oral dicloxacillin or oral cephalexin
- Wide-complex tachycardia → ventricular tachycardia (VT)
- Narrow-complex tachy → SVT
- Tx for SVT → vagal/carotid massage first; if doesn't work, then adenosine
- Tx of VT → anti-arrhythmics, e.g., amiodarone
- Tx of SVT or VT in setting of coma / unconsciousness → direct-current countershock
- Tx of first-degree heartblock or second-degree Mobitz I (Wenckebach) → observe
- Tx of second-degree Mobitz II or third-degree heartblock → pacemaker
- First-degree heartblock → PR-interval >200 milliseconds
- Mobitz I → gradually prolonging PR-interval before a QRS drops
- Mobitz II → no gradual prolongation of PR-interval; QRS randomly drops
- Third-degree → HR super slow at 30-40; no relation between p-waves and QRS complexes
- Infective causes of third-degree → Lyme disease, congenital lupus, diphtheria
- Give killed IM influenza vaccine when? → Every year in fall/winter only; start from 6 months of age
- Killed IM Influenza vaccine safe in pregnancy? → Yes, give anytime to pregnant women
- Live-attenuated intranasal influenza vaccine guidelines? → Only give age 2-49 to non-pregnant, non-immunocompromised persons
- Vaccines at age 2, 4, 6 months: HepB, Polio Salk, Pneumo PCV13, DPT, HiB, rotavirus (also give HepB at birth)
- HPV vaccine when → age 9-45
- Mom's HepB status unknown → give neonate HepB vaccine; only give immunoglobulin if mom comes back +
- MMR → first dose at 12-15 months; second dose age 4-6 years
- Varicella → one dose between 12-18 months
- Age 65 or older → give Pneumo PCV13 followed by PPSV23 6-12 months later
- Asplenia or sickle cell → PCV13 + PPSV23 + HiB + Meningococcal

- Circular lesion in pancreas seen in pancreatitis → pseudoabscess → answer = ERCP to drain internally
- Bullous changes on CXR or expanded lungs / hyperlucency → emphysema
- Centri-acinar emphysema → smokers
- Pan-acinar emphysema → alpha-1 anti-trypsin deficiency
- Young adult + non-smoker + has emphysema + relative died of hepatic cirrhosis → alpha-1 anti-trypsin deficiency
- CREST syndrome lung pathology? → can cause pulmonary fibrosis → pulmonary hypertension
- Restrictive lung disease → normal or increased FEV1/FVC
- Obstructive lung disease → decreased FEV1/FVC
- Why is FEV1/FVC normal or high in restrictive? → radial traction on outside of airways is sticky (keeps airways from closing)
- Apex to base lung changes when sitting/standing → **both** ventilation + perfusion increase apex to base
- Most common cause of otitis media → Strep pneumo
- Tx of otitis media → oral amoxicillin only
- Tx of recurrent OM → amoxicillin/clavulanate
- When to do tympanostomy tube → three or more OM in 6 months, or 4 or more in a year
- Most common cause of otitis externa → Pseudomonas
- Tx of otitis externa → topical ciprofloxacin + hydrocortisone drops
- Prevention of OE in someone with constant water exposure (e.g., crew team) → alcohol-acetic acid drops
- Tx of earwax buildup → carbamide peroxide drops
- Low hematocrit + low MCV + low transferrin + low TIBC + transferrin saturation normal or low → anemia of chronic disease
- Low hematocrit + low MCV + high transferrin + high TIBC + transferrin saturation super-low → iron deficiency anemia
- Low hematocrit + low MCV + increased red cell distribution width (RDW) → iron deficiency anemia
- Low hematocrit + low MCV + low/low-normal RDW → thalassemia
- Low hematocrit + low MCV + low iron + low ferritin → iron deficiency

- Low hematocrit + low MCV + normal iron + normal or high ferritin → thalassemia
- Low hematocrit + low MCV + normal iron + normal ferritin in pregnant woman on iron supplements → thalassemia
- Microcytic anemia that doesn't improve with iron supplementation → thalassemia
- Dx of thalassemia → hemoglobin electrophoresis
- Low hematocrit + normal MCV + low iron + normal or high ferritin → anemia of chronic disease
- Tx of anemia of chronic disease if renal failure is cause → answer = EPO
- Tx of anemia of chronic disease if renal failure not cause (IBD, RA, SLE, etc.) → CANNOT give EPO; Tx underlying condition.
- High BP + smoker + TIA or stroke or retinal artery occlusion. How to best decrease stroke risk → Answer = lisinopril, not smoking cessation
- Normotensive old pt + TIA or stroke or retinal artery occlusion → atrial fibrillation
- Hypertensive pt + stroke → do carotid duplex ultrasound
- Normotensive pt + stroke → do ECG; if ECG normal → Holter monitor
- High BMI female + irregular menstrual cycles → anovulation
- Anovulation + hirsutism → PCOS
- Anovulation. Cause USMLE wants? → insulin resistance → causes abnormal GnRH pulsation
- Why hirsutism in anovulation → abnormal GnRH pulsation causes high LH/FSH ratio
- Why high LH/FSH ratio important in anovulation/PCOS → ovulation stimulated when follicle not ready → no ovulation (anovulation) → follicle retained as cyst
- What's LH do? → Stimulates theca interna cells (females) and Leydig cells (males) to make androgens
- What's FSH do? → Stimulates granulosa cells (females) and Sertoli cells (males) to make aromatase; also primes follicles
- Tx for PCOS → if high BMI, weight loss first always on USMLE
- Tx for PCOS if they ask for meds and/or weight loss already tried → OCPs (if not wanting pregnancy); clomiphene (if wanting pregnancy)
- PCOS increases risk of what → endometrial cancer (unopposed estrogen)
- Tx of prostate cancer → flutamide + leuprolide together (if they force a sequence, choose F then L).
- Tx of acute gout → indomethacin (NSAID) first on USMLE; then steroids, then colchicine

- Tx of acute gout if indomethacin + steroids not listed → colchicine
- Tx of acute gout in pt with renal insufficiency or Hx of renal transplant → steroids
- Tx of chronic gout (decrease recurrence) → allopurinol or febuxostat (xanthine oxidase inhibitors)
- Never give which drug to pt with Hx of uric acid stones or over-producer → probenecid (uricosuric)
- What are rasburicase / pegloticase → urate oxidase analogues → cleave uric acid directly
- Young kid + self-mutilation + red-orange crystals in diaper → Lesch-Nyhan syndrome (X-linked)
- Lesch-Nyhan enzyme → HGPRT deficiency
- Crystal type in pseudogout → calcium pyrophosphate deposition disease
- Two main causes of pseudogout → primary hyperparathyroidism + **hemochromatosis**
- Two ways pseudogout presents → monoarthritis of large joint (i.e., knee) or **osteoarthritis-like presentation in someone with primary hyperparathyroidism or hemochromatosis**
- 32M + dark skin on forearms + increased fasting glucose; Dx? → hemochromatosis (bronze diabetes)
- Same male + painful hands + x-ray shows DIP involvement. Joint pain Dx? → **pseudogout**
- Tx of pseudogout → same as gout acutely; Tx underlying condition for chronic
- Biggest risk factor for osteoarthritis → obesity
- Tx of osteoarthritis → weight loss; if normal BMI → acetaminophen before NSAIDs
- Patient with OA taking naproxen (NSAID) + peripheral edema → increased renal retention of sodium
- Patient taking NSAID + edema; why? → NSAID decreases renal blood flow → PCT increases Na reabsorption to compensate for perceived low volume status → water follow sodium
- Tx of rheumatoid arthritis → Two-armed: symptom-relief + disease-modifying anti-rheumatic drugs (DMARDs)
- Symptom-relief for RA → NSAID first, then steroids (these do symptoms only; do not slow disease progression)
- DMARDs for early RA → always methotrexate first; if insufficient, add another DMARD (sulfasalazine or leflunomide); if insufficient add anti-TNF-alpha agent
- Methotrexate MOA → dihydrofolate reductase inhibitor
- Methotrexate side-effects → pulmonary fibrosis + hepatotoxicity + mouth ulcers (neutropenia)
- Sulfasalazine MOA → metabolized into sulfapyridine + mesalamine in the gut by bacteria
- Mesalamine is 5-ASA absorbed as the Tx for RA; only NSAID considered to be DMARD

- Leflunomide MOA → dihydroorotate dehydrogenase inhibitor (pyrimidine synthesis)
- Most specific Abs in RA → anti-CCP (cyclic citrullinated peptide), not RF (rheumatoid factor)
- X-ray of hands in RA vs OA → Only OA has DIPs involved; RA is PIPs + MCPs
- Symmetry in RA vs OA → RA is symmetrical; OA is not
- Any pt with red, warm, tender knee → joint aspiration (arthrocentesis); septic arthritis till proven otherwise
- Biggest risk factor for septic arthritis → abnormal joint architecture
- Pt groups most likely to get SA → prosthetic joints, RA/OA, recent intense exercise/joint trauma; peds (JRA)
- Pt group most likely to get SA → those with prosthetic joints (can't be more abnormal than fake joint)
- Pt with OA or RA has red, warm, tender knee → do arthrocentesis (septic arthritis)
- 17F had kickboxing tournament last weekend + knee is red, warm, tender → arthrocentesis (SA)
- Kid + recurrent knee redness, warmth, pain + fever → Juvenile rheumatoid arthritis (JRA; Still disease)
- Kid + recurrent joint pain +/- high ESR +/- rash → JRA
- Kid + recurrent joint pain + anemia → JRA (anemia of chronic disease)
- Kid with suspected JRA has sore knee → must do arthrocentesis to rule out septic arthritis
- Most common presentation finding in SLE → arthritis (>90%)
- Woman 20s-40s + arthritis + thrombocytopenia → SLE
- Woman 20s-40s + arthritis + mouth ulcer + circular skin lesions → SLE
- Malar rash + low RBCs + low WBCs + low platelets; mechanism for low cell lines? → increased peripheral destruction (antibodies against hematologic cells lines seen in SLE; isolated thrombocytopenia most common)
- Tx of SLE flare → steroids
- SLE + red urine; Dx? → lupus nephritis, more specifically, diffuse proliferative glomerulonephritis (DPGN)
- Histology of DPGN → wire looping capillary pattern
- Tx of lupus nephritis → mycophenolate mofetil
- Tx of discoid lupus → hydroxychloroquine
- Most specific Abs for SLE → anti-Smith (RNP), not anti-dsDNA

- Which Abs go up in acute SLE flares → anti-dsDNA (and C3 goes down)
- Drug-induced lupus Abs → anti-histone
- Drugs that cause DIL → Mom is HIPP → Minocycline, Hydralazine, INH, Procainamide, Penicillamine
- Viral infection + all three cell-lines are down → viral-induced aplastic anemia
- Viral-induced aplastic anemia; next best step in Dx? → bone marrow aspiration
- Viral-induced aplastic anemia; mechanism? → defective bone marrow production (contrast with SLE)
- Viral infection + low platelets → ITP (immune thrombocytopenic purpura)
- Woman 30s-40s with random bruising at different stages of healing → (also ITP; first rule out abuse)
- Mechanism of ITP → Abs against GpIIb/IIIa on platelets
- Dx of ITP → answer = low platelet count; don't choose increased bleeding time
- ITP Tx → steroids first, then IVIG, then splenectomy
- ITP episode → next best step in management → steroids
- ITP episode → most effective way to decrease recurrence → splenectomy (not first-line, but most effective)
- Family Hx of heme condition treated with splenectomy → hereditary spherocytosis (autosomal dominant)
- Bleeding time meaning? → platelet problem
- PT and aPTT meaning? → clotting factor problem
- Heme findings in ITP → increased BT, normal PT, normal aPTT
- Heme findings in hemophilia → increased aPTT; bleeding time and PT are normal
- Cause of hemophilia → X-linked recessive; hemophilia A (factor VIII def); hemophilia B (factor IX def)
- Tx of hemophilia A → desmopressin for hemophilia A (increases VIII release); then give factor VIII
- Tx of hemophilia B → give factor IX
- Classic hemophilia presentation → hemarthrosis in school-age boy; bleeding after circumcision in neonate
- Inheritance pattern of vWD → AD
- Heme findings in vWD → bleeding time always high; PT always normal; aPTT elevated half the time
- What is main function of vWF? → bridges platelet GpIb to underlying collagen (adhesion, not aggregation)

- What is secondary function of vWF → stabilizes factor VIII in plasma (that's why aPTT only half time increased)
- vWD presentation → always one platelet problem + one clotting factor problem
- Platelet problem? → epistaxis, bruising, petechiae → generally mild and cutaneous
- Clotting factor problem → menorrhagia, excessive bleeding with tooth extraction, hemarthrosis (but hemarthrosis very very rare in vWD; it is seen in hemophilia)
- vWD treatment → desmopressin → increases release of vWF
- Vitamin K deficiency heme parameters? → Increased PT + aPTT; bleeding time normal
- Cause of vitamin K deficiency in adults → chronic Abx knock out colonic flora
- Cause of sickle cell → glutamic acid to valine mutation on beta-chain
- Inheritance of sickle cell → AR
- Nephrotic syndrome in SS → FSGS
- Dark urine in SS → renal papillary necrosis
- HY drugs that cause agranulocytosis → clozapine, ganciclovir, propylthiouracil, methimazole, methotrexate, ticlopidine
- How will agranulocytosis (neutropenia) present on USMLE? → mouth ulcers + fever
- Tx for febrile neutropenia / neutropenic fever → immediate broad-spectrum IV Abx
- Broad-spectrum Abx example? → Piperacillin/tazobactam; cefepime + vancomycin
- What is ganciclovir used for? → Tx of CMV (DNA polymerase inhibitor)
- PTU and methimazole are used for what? → Tx of Graves
- Ticlopidine is what? → ADP2Y12 blocker anti-platelet agent (clopidogrel, prasugrel, ticagrelor also)
- Strongest indication for anti-coagulation → prosthetic material in heart / prosthetic valve (factoid in isolation)
- "Hot feels cold; cold feels hot" (temperature dysesthesia) → ciguatera toxicity → toxin blocks sodium channels → caused by consumption of reef fish (mahimahi, Spanish mackerel, etc.)
- Pt with no prior Hx of atopy/asthma + eats meaty fish in sketch location (e.g., Bali) + develops dyspnea + allergic-like reaction → answer = scombroid, not seafood allergy → histidine decarboxylase in decaying fish convert histidine to histamine → allergic-like reaction (often misdiagnosed as allergy)

- Pt gets allergic-like reaction after eating shellfish → answer = shellfish allergy, **not** scombroid
(students get all trigger-happy about scombroid after learning about something new, weird, and cool, but if on the USMLE they say shellfish, it's **shellfish allergy, not scombroid**)
- Vomiting a few hours after eating meat → *S. aureus* preformed heat-stable toxin
- Vomiting (or any unusual Sx like bloody diarrhea) + eating custards, creams, potato salad → answer = *S. aureus* preformed HS toxin → the type of food in this scenario “wins” over the weird bloody diarrhea finding → bear in mind typical bloody-diarrhea-inducing gram (-) rods like EHEC, *Yersinia enterocolitica*, *Campylobacter*, *Shigella*, *Salmonella* have **~1-3-day incubation period**) → iow, if you get sick on the scale of hours from food, *S. aureus* preformed toxin is likely
- Tx of otitis externa → topical ciprofloxacin + hydrocortisone drops
- Prophylaxis for otitis externa (i.e., in someone with continued water exposure, like crew) → topical alcohol-acetic acid drops
- Tx for cerumen buildup → carbamide peroxide drops
- Most common cause of otitis externa → *Pseudomonas*
- Otitis externa + mastoiditis → malignant otitis externa
- Mx of malignant otitis externa → CT or MRI of temporal bone because pus collection is common; if don't rule out fluid collection and drain it appropriately, can cause brain abscess; this is on one of the pediatric NBME forms, where the answer was CT of the temporal bone in a two-year-old, which is an outrageous dose of radiation for a kid, but it's the answer on the form; in UW for 2CK, they didn't list CT, but had MRI and x-ray as answers, and MRI was correct; apparently x-ray is insufficient; mastoiditis will classically present in kid with a pinna that's displaced upward and outward, often with him or her pulling on it bc of the pain.
- Tx of otitis media → amoxicillin (amoxicillin/clavulanate [Augmentin] is the wrong answer initially; use Augmentin for recurrent OM)
- When to do a tympanostomy tube? → 3+ OM in a 6-month period or 4+ in a year
- Tx for Strep pharyngitis? → Amoxicillin or penicillin only (not Augmentin)
- Aspiration pneumonia or pulmonary abscess; which antibiotic should be given? → clindamycin (anaerobes above the diaphragm)
- Curs and cups of foul-smelling sputum in COPD, TB, or CF patient → bronchiectasis

- Most common cause of bronchiectasis → worldwide: TB; in western countries: CF
- Young kid + scant white sputum + linear opacity in right-middle lobe on CXR; Dx? → **answer = bronchiectasis caused by right middle lobe syndrome** (no I am not fucking with you; this is on one of the pediatric 2CK forms → 1st question I've ever seen of bronchiectasis where it wasn't cups and cups of foul-smelling sputum; also, if you Google, it, there literally is a peds condition called right middle lobe syndrome that leads to bronchiectasis → search it over some tacos and a Samuel Adams and knock yourself out)
- Chromosome for AR and AD polycystic kidney disease → 6 for AR; 16 for AD
- ADPKD → which do we do for screening, MR angiogram circle of Willis, or serial blood pressure checks? → answer = serial blood pressure checks → don't do MR angiogram screening unless FHx of aneurysm → most patients get high blood pressure from cyst impingement on renal microvasculature → RAAS surges
- Most common extra-renal location for cysts → liver
- Important point about AR: shows up in peds + causes hepatic fibrosis
- Important point about AD: presents in adults; cysts present from birth but just grow + become symptomatic ages 30-40+.
- Empiric Abx therapy for meningitis → ceftriaxone + vancomycin (+/- steroids)
- Lumbar puncture or Abx first in suspected meningitis? → new guidelines say LP first
- When do you do CT head before LP in suspected meningitis?
 - Confusion that interferes with neurologic exam / decreased GCS score
 - Seizure
 - Focal neurologic signs (motor or sensory)
 - Papilledema or if the optic fundi cannot be visualized
 - Above reasons indicate potential mass lesion, where if you do an LP you can cause tonsillar herniation and death; if CT negative, proceed cautiously to LP
- Bacterial meningitis: low glucose, high protein, high neutrophils (polymorphonuclear cells; PMNs)
- Aseptic (viral) meningitis: normal glucose, normal (or slightly elevated) protein, high lymphocytes
- Fungal meningitis: low glucose, high protein, high lymphocytes (similar to bacterial, but high lymphocytes instead of neutrophils)

- Herpes encephalitis: **lots of RBCs in CSF due to temporal lobe hemorrhage** → CT is often negative, but sometimes Q will mention wave slowing or temporal complexes on EEG
- Difference between meningitis and encephalitis → meningitis is nuchal rigidity (neck stiffness) + photophobia + ophthalmoplegia; encephalitis presents with **confusion**
- Dx of Cryptococcal meningitis? → answer = **latex agglutination** if it's listed over India ink; mucicarmine staining (red stain) can also be done
- Tx for Cryptococcal meningitis → amphotericin B + flucytosine, followed by fluconazole taper
- Nodular density in upper lobe in immunocompromised pt → aspergilloma → next best step = open lung biopsy (sounds radical, but it's the answer on one of the NBME forms) → Tx with -azole → invasive aspergillosis can be treated with caspofungin or voriconazole
- 22M + Hx of three bacterial pneumonias + atopy; presents today with a sore left cheek; Dx? → IgA deficiency (student says "wtf?") → firstly, sore cheek is sinusitis → IgA deficiency is recurrent sinopulmonary infections that "aren't that bad" in a patient "not that young" (that is, it's not a super-sick three-year-old like in SCID or Bruton) → **can present with autoimmune phenomena like atopy and vitiligo**; also can present with Hx of *Giardia* → apparently NBME is also now testing that IgA deficiency at the same time as Celiac disease means that we can't measure IgA anti-tissue transglutaminase reliably because clearly the patient wouldn't make the IgA → anaphylaxis after blood transfusion is super HY for IgA deficiency, but also too easy and not mentioned in most Qs.
- Most common immunodeficiency in humans → IgA deficiency
- 17F + 1-year Hx of autoimmune thyroiditis + 2-year Hx of type I DM + Candidal infections since childhood; Dx? → chronic mucocutaneous candidiasis → two points: 1) clearly the Candidal infections can't be due to the diabetes if she's had them since childhood and only DM for two years; 2) USMLE likes "autoimmune conditions go together," the same way it likes "autoimmune conditions and immunodeficiencies go together"; in other words, CMC and IgA deficiency are examples of immunodeficiencies with an autoimmune origin, so the vignette mentioning autoimmune phenomenon isn't an accident.
- Dx of PJPneumonia → bronchoalveolar lavage
- When to add steroids to TMP/SMX for PJP? → A-a gradient >35 or pO₂ <60 mm Hg
- 36M + long-bone fractures + petechiae on the chest → fat embolism

- Motor vehicle accident (MVA) + paradoxical breathing (chest moves outward with exhalation; inward with inhalation) → flail chest
- MVA + rib fractures + underlying infiltrates in lung + low O2 sats → pulmonary contusion
- MVA + no rib fractures + non-central chest pain + pulmonary infiltrates underlying the painful area → pulmonary contusion (resources will say “white out of the lung” for pulmonary contusion, but this is buzzwordy and never shows up on actual NBME material)
- MVA + pulmonary infiltrates + low O2 sats + bolus of normal saline given, resulting in worsening of O2 sats → pulmonary contusion (contused lung is very sensitive to fluid overload)
- MVA + **bruising/pain over the sternum** +/- rib fractures → myocardial contusion
- MVA + bruising/pain over sternum + pulmonary infiltrates + O2 sats get worse when saline is given → answer = myocardial contusion (“Wait, but I thought you said that latter finding means pulmonary contusion” → it does, and it’s HY for pulmonary contusion, but “bruising/pain over the sternum” wins if it’s listed; this is on a 2CK NBME)
- Important point about Mx of myocardial contusion → do troponins + must monitor for arrhythmia
- Adult male + abdo pain + Hx of alcohol use + diffuse pulmonary infiltrates + low O2 sats → ARDS
- ARDS must have $pO_2/FiO_2 < 300$
- Tx of ARDS → **low-tidal volume mechanical ventilation** (prevents barotrauma) + increase PEEP
- When you get a random ventilator Q and they want an answer → “increase PEEP” almost always right
- Patient has improving O2 sats on ventilator; next best step? → “wean from ventilator”
- Thyroid dysfunction on ventilator → euthyroid sick syndrome → normal TSH, normal T4, low T3, high reverse T3 (cortisol decreases peripheral conversion of T4 to T3, allowing more to go to reverse T3)
- Wtf is reverse T3? → an inactive form of T3; all you need to know is that if T4 goes up (e.g., in Graves), reverse T3 should be up because T4 will convert to both T3 and reverse T3; it is also elevated in euthyroid sick syndrome (and T3 down!)
- 25F + intermittent bloody diarrhea for 3 months + intermittent fever + weight loss → answer IBD (Crohn or UC)
- Tx for Crohn + UC → USMLE wants oral sulfasalazine (or mesalamine) first before oral steroids; for perianal disease in Crohn, topical agents / enemas can be used; NBME won’t make you pick between oral and topical distinguish (that’s more Qbank being pedantic); surgery can be done for UC

- UC + high bilirubin + high ALP → primary sclerosing cholangitis
- Red shins + Crohn → erythema nodosum (type III hypersensitivity; panniculitis → inflammation of subcutaneous fat, not a rash)
- Crater with necrotic debris on forearm + UC → pyoderma gangrenosum
- IBD + eczematoid plaque on forehead + sore joints → psoriatic arthritis (HLA-B27 → PAIR → Psoriasis, Ankylosing spondylitis, IBD, Reactive arthritis)
- IBD + back pain → sacroiliitis (or ankylosing spondylitis)
- Biopsy in Crohn → non-caseating granulomas; transmural; UC you don't see these findings
- Vesicles anywhere on body (not limited for extensors) + Celiac → dermatitis herpetiformis
- Biopsy of DH → IgA deposition at dermal papillae
- Biopsy of small bowel in Celiac → flattening of intestinal villi
- Dx of Celiac → IgA anti-tissue transglutaminase, anti-gliadin (aka anti-endomysial)
- After Celiac Ab positivity, what's the next best step (no further intervention necessary or duodenal biopsy) → answer = duodenal biopsy (sounds wrong, but it's what USMLE wants)
- Weird factoid about Celiac → increased risk of T cell lymphoma
- Biopsy of small bowel in lactose intolerance → normal villi
- Dx of lactose intolerance → hydrogen breath test or decreased stool pH
- Vague vignette where it sounds like either Celiac or lactose intolerance but it's in a young adult who's had zero symptoms until now → lactose intolerance (can be adult-onset)
- PAS-positive macrophages in the lamina propria + arthritis → Whipple disease
- AIDS patient with CD4 count of 47 + confluent ulcers seen on colonoscopy → CMV colitis → confluent means "linear" → CMV = linear ulcers; HSV = punched-out ulcers
- Tx for CMV → ganciclovir (DNA polymerase inhibitor)
- Toxicity of ganciclovir → neutropenia (mouth ulcers + fever)
- Tx of herpes → acyclovir
- Toxicity of acyclovir → nephrotoxicity (crystal nephropathy → acyclovir stones not visible on CT)
- Hereditary angioedema → due to C1 esterase **inhibitor** deficiency
- Tx for HA → danazol (synthetic androgen receptor partial agonist that causes liver to make more C1EI)

- Don't give which drugs to patients with HA → ACEi (can cause angioedema)
- Familial thyroid cancer → medullary (even if they mention nothing else related to MEN 2A/2B); apple-green birefringence on Congo red stain due to amyloid deposition; serum calcitonin high
- Calcitonin mechanism of action → inhibits osteoclast activity (**not** the opposite of PTH; in other words, doesn't put calcium back into bone; it merely caps the Ca that can resorb out of the bone)
- Most common thyroid cancer → papillary; extends lymphatogenously; has papillary structure and psammoma bodies on LM; don't worry about buzzywordy things like Orphan Annie nuclei
- Follicular carcinoma → literally just thyroid follicles on biopsy; will be a cold nodule, like any other type of thyroid cancer (for instance, if you see follicles but it's a hot nodule w/ increased uptake, that's a toxic adenoma, rather than follicular thyroid cancer); spreads hematogenously
- Hashimoto + thyroid cancer + no other histo description → thyroid lymphoma → autoimmune diseases increase the risk of non-Hodgkin lymphoma
- MEN1 → pituitary, pancreas, parathyroid (MEN1 gene; chromosome 11)
- MEN2A → parathyroid, medullary thyroid carcinoma, pheochromocytoma
- MEN2B → medullary thyroid carcinoma, pheochromocytoma, mucosal neuromas, Marfanoid body habitus ("oid" means looks like but ain't)
- Riedel thyroiditis → fibrosis of thyroid → can extend into adjacent structures, e.g., the esophagus, and resemble anaplastic carcinoma
- 52M + abdominal mass + weight loss + biopsy shows lymphocytes + interspersed macrophages → Burkitt lymphoma (student says: "Wtf? I thought Burkitt was the African boy with a jaw lesion." Yeah, but in Western countries, Burkitt is usually intra-abdominal; even new studies in Africa have shown a growing preponderance of intra-abdominal Burkitt)
- Translocation for Burkitt → t(8;14), but USMLE also wants you to know t(2;8) and t(8;22)
- Gene for Burkitt → c-myc → transcription factor
- Translocation for CML → t(9;22) → Philadelphia chromosome
- What is the product of the t(9;22) → bcr/abl tyrosine kinase inhibitor
- Tx for CML → imatinib (tyrosine kinase inhibitor)
- Side-effect of imatinib → fluid retention (edema)

- What do you see on bloods in CML → high leukocyte count (mature neutrophils + metamyelocytes + myelocytes)
- Translocation for APL (AML M3) → t(15;17)
- What do you see on blood smear in APL → Auer rods
- What are Auer rods composed of? → myeloperoxidase (cause DIC when released into blood during Tx)
- Translocation for follicular lymphoma → t(14;18)
- Gene for follicular lymphoma → bcl-2 → anti-apoptotic molecule
- Most common indolent non-Hodgkin lymphoma → follicular (waxing and waning neck mass over two years in an adult)
- Most common aggressive NHL → diffuse-large B cell lymphoma (DLBCL)
- Translocation for mantle cell lymphoma → t(11;14)
- 17F + painless lateral neck mass + mediastinal mass; Dx? → Hodgkin lymphoma
- 42M + painless lateral neck mass + hepatomegaly; Dx? → Hodgkin lymphoma
- 40M + Hodgkin lymphoma + renal condition → minimal change disease (“Wtf? Isn’t that kids after viral infection?” → It’s also seen in Hodgkin due to a cytokine effect for whatever magical reason; in UW for 2CK actually)
- Biopsy of lymph node in Hodgkin → Reed-Sternberg cells (“owl eyes” → CD15/30+ B cells)
- Are lymphomas / leukemias normally B or T cell? → almost always B cell
- When is the answer T cell? → When pt has a thymic lesion as evidenced by a positive Pemberton sign (flushing of face with arms above the head) → mediastinal mass in Hodgkin is due to mediastinal lymph node enlargement, not a thymic mass (thymic lesion in Hodgkin exceedingly rare)
- First drug to start in T2DM → metformin
- Side-effect of metformin → lactic acidosis
- Mechanism of metformin → “increases glycolysis; decreases gluconeogenesis”
- Tx of impetigo → topical mupirocin
- Tx of erysipelas + cellulitis → oral dicloxacillin or oral cephalexin
- Inpatient Tx of MSSA → IV flucloxacillin or IV cephazolin

- Tx of osteomyelitis → IV nafcillin or IV oxacacilin or IV cephazolin; add ceftriaxone in sickle cell; add clindamycin in MRSA
- Tx of MRSA skin infection → clindamycin, or TMP/SMX, or doxycycline, or linezolid → vanc has poor skin penetration
- Suspected incarcerated hernia in a vignette → answer = immediate groin exploration
- Most common cause of fever after surgery → atelectasis
- Electrolyte abnormality in Cushing syndrome → hypokalemia (chronically high glucocorticoid can cause potassium wasting distally in the kidney similar to aldosterone)
- Pt has tachy + diaphoresis + diarrhea after drug → serotonin syndrome (tramadol; MOA too soon after stopping SSRI)
- Pt has tachy + diaphoresis + diarrhea + tricuspid valve lesion → carcinoid syndrome
- Cause of carcinoid syndrome → usually small bowel or appendiceal tumor that has metastasized to liver (if not metastasized, liver can process serotonin derivatives it receives); can also be due to bronchogenic carcinoid; tumors are S-100 positive and of neural crest origin
- Dx of serotonin + carcinoid syndromes → urinary 5-hydroxyindole acetic acid (5-HIAA)
- Tx of serotonin syndrome → remove offending agents + administer cyproheptadine (serotonin receptor antagonist)
- Tx of carcinoid syndrome → Tx underlying condition
- Asthma (outpatient) → albuterol (short-acting beta-2 agonist; SABA) inhaler for immediate Mx → if insufficient, start low-dose ICS (inhaled corticosteroid) preventer → if insufficient, maximize dose of ICS preventer → if insufficient, add salmeterol inhaler (long-acting beta-2 agonist; LABA); in other words:
 - **1) SABA; then**
 - **2) low-dose ICS; then**
 - **3) maximize dose ICS; then**
 - **4) LABA.**
- That initial order is universal. Then you need to know last resort is **oral corticosteroids, however they are most effective.** In other words:
- 12M has ongoing wheezing episodes + is on albuterol inhaler; next best step? → add low-dose ICS

- 12M has ongoing wheezing episodes + is on albuterol inhaler; what's most likely to decrease recurrence → oral corticosteroids (student says "wtf? I thought you said ICS was what we do next and that oral steroids are last resort" Yeah, you're right, but they're still **most effective** at decreasing recurrence. This isn't something I'm romanticizing; this distinction is assessed on the NBME forms.
- After the LABA and before the oral steroids, any number of agents can be given in any order – i.e., nedocromil or cromolyn sodium, zileuton, montelukast, zafirlukast.
- MOA of nedocromil and cromolyn sodium → mast cell stabilizers
- MOA of zileuton → lipoxygenase inhibitor (enzyme that makes leukotrienes from arachidonic acid)
- MOA of the -lukasts → leukotriene LTC, D, and E4 inhibitors. LTB4 receptor agonism is unrelated and induces neutrophilic chemotaxis (LTB4, IL-8, kallikrein, platelet-activating factor, C5a, bacterial proteins)
- 16M goes snowboarding all day + takes pain reliever for sore muscles afterward + next day develops wheezing out on the slopes again; what's going on? → took **aspirin + this is Samter triad** (now clumsily known as aspirin-exacerbated respiratory disease [AERD]) → triad of aspirin-induced asthma + aspirin hypersensitivity + **nasal polyps**. Just to be clear, other NSAIDs can precipitate Samter triad, but the literature + USMLE will make it explicitly about aspirin.
- 16M takes aspirin + gets wheezing; what are we likely to see on physical exam? → answer on USMLE = nasal polyps.
- "Wait I don't understand. Why would aspirin cause asthma?" → arachidonic acid can be shunted down either the cyclooxygenase or lipoxygenase pathways; if you knock out COX irreversibly by giving aspirin (or reversibly with another NSAID), more arachidonic acid will be shunted down the lipoxygenase pathway → more leukotrienes → more bronchoconstriction
- Kid has Hx of AERD; physician considers agent to decrease his recurrence of Sx → zileuton, or -lukasts (both are correct; and only one will be listed).
- Kid has Hx of AERD; what agent is most likely to decrease his recurrence of Sx → **oral steroids** (sounds wrong, but once again, you need to know oral steroids are most effective for preventing asthma, period; this is exceedingly HY, especially on 2CK forms). We simply don't want to give them because of their nasty side-effects (Cushing syndrome).

- Any weird asthma Tx? → **omalizumab** → monoclonal antibody against IgE → used for intractable, severe asthma unresponsive to oral steroids + in patients who have eosinophilia + high IgE levels (I asked a pulmonologist about this drug years ago when I was in MS3 and he said he was managing 1000 patients with asthma and just three were on omalizumab).
- Acute asthma Mx (emergencies) → most important piece of info straight-up is: USMLE wants you to know that inhaled corticosteroids (ICS) have **no role in acute asthma management**. First thing we do is give oxygen (any USMLE Q that shows depressed O2 sats, answer is always O2) + nebulized albuterol (face mask with mist); **IV steroids** are then administered. The Mx algorithm is more complicated, but that is what you need for the USMLE.
- Acid-base disturbance in asthma? → respiratory alkalosis → **low O2, low CO2, high pH, normal bicarb**
- “Wait, why the low CO2? Aren’t you not able to breathe?” → low CO2 is due to high respiratory rate; even if your bronchioles are constricted + filled with secretions, CO2 can diffuse really quickly; in contrast, O2 diffuses slowly and requires healthy airways; that’s why with a high RR, O2 and CO2 are both low (O2 can’t get in, but CO2 can still get out); 19 times out of 20 on the USMLE, if your respiratory rate is high, CO2 is low.
- “19 times out of 20? Then what’s the exception.” → I’ve seen COPD questions where the patient will have a RR of 28 but a super-high CO2, and the answer is chronic respiratory acidosis + acute respiratory acidosis (acute on chronic) → in the event of emphysema, where you literally have reduced surface area for gas exchange, even if your RR is high, CO2 has no way of diffusing out.
- “Wait, why is bicarb normal in acute asthma attack? Shouldn’t it go low to compensate if CO2 is low?” → not enough time for bicarb to change; takes a minimum of 12-24 hours for renal elimination to have an effect on serum levels; this is why in altitude sickness, where CO2 is low (due to high RR bc of lower atmospheric O2), acetazolamide (carbonic anhydrase inhibitor) can be given to increase bicarb loss in the PCT of the kidney to essentially force a metabolic acidosis to compensate.
- 12M + acute asthma episode + given O2 + nebulized albuterol + IV steroids + his acid-base disturbance is as we talked about above → after 30 minutes, new values are: low O2, normal CO2, normal pH, normal bicarb; why? → he’s getting tired → low O2 means he should still be hyperventilating, so for CO2 and pH to have normalized means his RR is decreasing → **answer on USMLE = intubate**. When O2 and CO2 are both initially down, that’s called a type I respiratory failure;

then eventually it will invert, where this patient will have a respiratory acidosis with low O₂, high CO₂, low pH, normal bicarb (type II respiratory failure when O₂ and CO₂ are the opposite).

- Acid-base disturbance in pulmonary embolism? → same as acute asthma: **low O₂, low CO₂, high pH, normal bicarb.**
- Tx of pulmonary embolism → heparin before spiral CT; do V/Q scan in pregnant women.
- In pregnant women, if V/Q scan shows segmental defect; what's the next best step in Dx? → answer = spiral CT → "Wait, but I thought we don't do CT in pregnant women." You're right. We don't. But if for whatever magical reason they ask you what the next best step in Dx is after the V/Q scan is positive, the answer is CT. It doesn't mean we're going to do it. But it's the answer. And this is in UW for 2CK.
- Pt has PE and is already on warfarin → answer = don't give heparin; go straight to spiral CT.
- What about IVC filter? → After the spiral CT confirms the PE, an IVC filter can be inserted in a patient **who's already anticoagulated.** The tricky part is, **don't select IVC filter before doing the CT to confirm.** Students will memorize IVC filter as the answer in someone who's already on warfarin, but think about it: you're not going to stick a fucking filter in someone's IVC before at least confirming the PE with the spiral CT.
- What about tPA in PE? → Never an answer on the USMLE because the indications are debated.
- Is tPA ever an answer for anything? → Ischemic stroke within 4.5 hours. Must do non-contrast CT of the head to confirm no bleed before giving tPA.
- 72M has 30 minutes of facial drooping + arm weakness since waking up from a nap → amount of time since stroke = amount of time that has passed since he was last known to be normal (**i.e., before he went to sleep**) → on the USMLE, this situation often means **don't give the tPA.**
- Regarding contraindications for tPA on the USMLE: most important one is BP, which is 185/110 (if either value is exceeded, don't give tPA). There are many contraindications, but other HY ones are low platelets, high PT or aPTT; Hx of GI bleed past 21 days; Hx of intracranial bleed; recent major surgery.
- 45F + alcoholic + increased creatine kinase → rhabdomyolysis (increased risk in alcoholics)
- 82F + fell in her house + positive for blood on urine dipstick + negative for RBCs on urine LM → rhabdomyolysis (myoglobinuria causes false-positive blood on dipstick)

- Anemia in alcoholism? → non-megaloblastic macrocytic anemia (USMLE will give you high MCV [normal is 80-100] in alcoholic with a bunch of other things going on, and they merely want you to know his high MCV is due to the alcohol)
- Electrolyte abnormality in rhabdo → hyperkalemia (cell lysis + renal failure → myoglobin causes acute tubular necrosis)
- Woman has episiotomy posterior in the midline (vaginal incision made to allow for fetus's head to pass through birth canal without causing vaginal laceration); if the doctor cuts too far, what will he cut into? → **answer = external anal sphincter**
- Stress incontinence → weakened pelvic floor muscles resulting in loss of urine with increased abdominal pressure (coughing, sneezing, laughing) → Hx of multiple pregnancies classic, but often too easy of a descriptor and they won't say that → they'll say there's "downward movement of the vesicourethral junction with coughing"; next best step in Mx? → pelvic floor (Kegel) exercises → if insufficient, do mid-urethral sling; **do not** give medications for stress incontinence (HY!).
- USMLE might ask you which muscle is **not** strengthened by Kegel exercises → student then proceeds to have two thoughts: 1) "wtf, I'm supposed to know Kegel exercises at that high level of detail?" and 2) couldn't *any* muscle not be strengthened by Kegel exercises; I mean, the deltoid wouldn't be for instance." → **answer to this Q = internal anal sphincter** → even if you have zero clue about Kegel exercises, bear in mind **internal sphincters (urethral + anal) are under sympathetic control** → **you can't voluntarily strengthen a muscle not under somatic (voluntary) control**; in case you're curious though, Kegel strengthens levator ani (which comprises pubococcygeus, puborectalis, and iliococcygeus).
- Urge incontinence → answer = "hyperactive detrusor," or "detrusor instability" → needs to run to the bathroom when sticking a key in the front door; needs to run to bathroom when opening car door; answer in multiple sclerosis + menopause (part of vasomotor Sx); can be idiopathic; answer = give oxybutynin (anti-muscarinic) or mirabegron (beta-3 agonist); **once again, do not give these drugs in stress incontinence.**
- Overflow incontinence → answer in diabetes and BPH → neurogenic bladder caused by myelin damage from sorbitol (glucose enters myelin, causing osmotic damage); in BPH, merely due to outlet obstruction → leads to detrusor burnout; **in overflow incontinence, postvoid volume is high (i.e.,**

300-400 mL in USMLE Qs); normal should be <50-75 mL; for diabetic bladder, answer = bethanecol (muscarinic agonist); for BPH, **insert catheter first always.**

- 82M + dribbling, hesitancy, interruption of urinary stream + suprapubic mass (bladder) + bacteria in the urine → answer = insert catheter first, not antibiotics
- 25F + 6 weeks of dysuria + anterior vaginal wall pain + urinary findings normal → answer = chronic interstitial cystitis; must have 6+ weeks of Sx in the absence of any findings; anterior vaginal wall pain sounds weird, but it's on the obgyn NBME forms, and something to bear in mind is that a cystocele (unrelated) will protrude through the anterior superior vaginal wall, so the anatomic proximity is known to cause symptomatology.
- Detrusor muscle → contracts under parasympathetic activity via the pelvic splanchnic nerves (S2-S4); when not voiding, detrusor muscle is kept relaxed by sympathetic activity via the inferior hypogastric nerves (T10-L1).
- Internal urethral sphincter → kept closed by sympathetic activity via inferior hypogastric nerves (T10-L1).
- External urethral sphincter → Opened by somatic activity via the pudendal nerve (S2-4)
- 40M goes hiking + linear vesicles on calf appearing days later → answer = contact dermatitis = type IV hypersensitivity; **linear vesicles** = poison ivy/sumac
- 38F gardens a lot + gets rash on face, arms, backs of hands → answer = contact dermatitis from sunscreen
- Type I HS → **fast-onset; anaphylaxis; atopy (asthma, hay fever [rhinoconjunctivitis], eczema);** two IgEs bind antigen at Fab fragments + move into close proximity and crosslink → mast cell degranulates + secretes histamine; answer for drug rashes that occur soon after receiving the drug (e.g., sulfa); treat anaphylaxis with IM epinephrine (beta 2 agonism opens the lungs; NE doesn't act on beta 2)
- Type II HS → autoantibodies against one's own cells + receptors
 - **Heparin-induced thrombocytopenia (HIT;** Abs against platelet factor 4-heparin complex) → treat by stopping heparin + giving direct-thrombin inhibitor (i.e., dabigatran or lepirudin); warfarin is the wrong answer
 - **Graves disease** → activating TSH Abs against TSH receptor

- **Goodpasture syndrome** → “2, 3, 4... 2, 3, 4... 2, 3, 4. The Goodpasture is marching in the field, 2, 3, 4!” → Type 2 hypersensitivity against the alpha-3 chains of type 4 collagen
- **Pernicious anemia** → Abs against intrinsic factor or parietal cells → decreased B12 absorption through terminal ileum
- **Warm autoimmune hemolytic anemia** → Coomb positive, meaning IgG targets RBCs → seen in things like ABO mismatch, drugs/infection; CLL
- **Cold autoimmune hemolytic anemia** → IgM Abs against RBCs → classically Mycoplasma
- **ITP (immune thrombocytopenia purpura)** → Abs against GPIIb/IIIa on platelets → low platelet count + high bleeding time → treat with steroids, then IVIG, then splenectomy
- Type III HS → Ab-Ag complexes
 - **Serum sickness** → immune complexes depositing in joints several days after drug or infection
 - **Arthus reaction** → localized cutaneous type III HS → skin reaction/rash at injection site several days after administration of agent → key point is that it’s not immediate; in type I hypersensitivity, we’d get an immediate reaction; in Arthus reaction, it takes a few days
 - Super HY is **postinfectious arthritis** → arthritis due to HepB, HepC, rubella, Yersinia enterocolitica, etc. → immune complex deposition in joints → this is considered a serum sickness
 - **Erythema nodosum** → panniculitis (inflammation of subcutaneous fat) due to immune complex deposition → USMLE likes **Crohn disease**, sulfa drugs, Strep infections, and Coccidioidomycosis as causes.
 - **Post-streptococcal glomerulonephritis (PSGN)** → can occur after skin infections as well (i.e., impetigo, erysipelas, cellulitis)
- Type IV hypersensitivity → T cell-mediated response (delayed)
 - Contact dermatitis (nickel [wristwatches], sunscreen, poison ivy/sumac, rubber)
 - PPD test for TB
 - Multiple sclerosis (T cell attack against oligodendrocytes in white matter)
 - Stevens-Johnson syndrome; toxic epidermal necrolysis

- Need to know low bicarb in pt with dehydration (or any type of shock) → answer = lactic acidosis → decreased perfusion to vital organs → decreased oxygen delivery → increased anaerobic respiration → increased lactic acid
- High-anion gap metabolic acidosis → MUDPILES → methanol, uremia, DKA, phenformin, iron/INH, lactic acidosis, ethylene glycol, salicylates
- Tx for ethylene glycol and methanol toxicity → fomepizole **only** if listed → in other words, if you get combinations with “ethanol first then fomepizole,” etc., just choose “**fomepizole only**” if it’s listed
- Paint thinner + blurry vision → methanol toxicity (on one of the NBMEs)
- Which decreases risk of stroke more, smoking cessation or BP control? → BP control (USMLE wants lisinopril as the answer, not smoking cessation); for stroke, answer is always hypertension as worse risk factor
- High HbA2 → answer = beta-thalassemia
- Dx of alpha or beta thalassemia → hemoglobin electrophoresis
- Pregnant woman has low serum iron that doesn’t improve with iron supplementation → answer = do hemoglobin electrophoresis → Dx = thalassemia (usually alpha trait with one mutation because that’s asymptomatic)
- Dx of sickle cell → hemoglobin electrophoresis
- Dx of multiple myeloma → serum protein electrophoresis, then bone marrow biopsy
- Adult male + works in manufacturing/factory + cognitive decline + microcytic anemia → answer = lead poisoning → inhibits delta-ALA dehydratase + ferrochelatase → **microcytic anemia is really HY for lead poisoning** → will often see basophilic stippling or RBCs
- What kind of RBCs in thalassemia → target cells
- Infection + RBCs lacking central pallor + positive Coomb test → answer = hemolytic anemia, **not** hereditary spherocytosis → spherocytes are seen in drug- and infection-induced hemolytic anemia, not just in HS → difference is Coomb (IgG against RBCs) is positive in Ab-induced hemolytic anemia, but clearly not in HS bc the latter is cytoskeletal (ankyrin, spectrin, band protein deficiency) in etiology.
- 12M + red urine 1-3 days after upper respiratory tract infection (URTI) → IgA nephropathy, not PSGN; can also get IgA nephropathy from GI infections

- 12M + red urine 1-2 weeks after URTI or skin infection → PSGN → can get it from Group A Strep skin infections
- 6F + red urine + abdo pain + arthralgias + violaceous lesions on buttocks + thighs; Dx? → Henoch-Schonlein purpura; red urine = IgA nephropathy → HSP is tetrad of 1) IgA nephropathy, 2) palpable purpura, 3) arthralgias, 4) abdo pain
- 23F + unilateral resting tremor + hemolytic anemia + increased LFTs; next best step in Mx? → **answer = do a slit-lamp exam** → Dx = Wilson disease; Parkinsonism in a young patient = Wilson disease until proven otherwise → low serum ceruloplasmin + increased urinary copper
- How is copper normally excreted by the body? → through bile; defective excretory pump in Wilson
- Tx for Wilson disease → penicillamine
- Tx for hereditary hemochromatosis → serial phlebotomy
- Tx for secondary hemochromatosis (transfusional siderosis) due to chronic blood transfusions → chelation therapy
- Pink line tracking up the arm from the palm in 35M who burned himself recently; Dx? → lymphangitis → sporotrichosis is wrong answer (can cause lymphatogenous spread)
- Brown recluse spider bite → abdominal pain; manage symptomatically
- Black widow spider bite → causes hypocalcemia → give IV calcium gluconate
- Woman who works in dental care with vesicle on finger; Dx? → herpetic whitlow → HSV1/2 of the finger → treat with oral acyclovir (in real life will give both oral and topical; on the USMLE, answer is always oral)
- Suspected skin cancer in non-cosmetically sensitive area → surgical excision
- Suspected skin cancer on face → Mohs surgery (thin slices looking for positive margins)
- Suspected skin cancer on neck → full-thickness biopsy
- Most important prognostic factor for melanoma → **depth** of lesion
- Recommendation to prevent melanoma → avoid sun or use protective clothing (sounds absurdly obvious, but I've seen students choose wrong answers like use SPF30)
- Farmer/fisherman/construction worker + red, scaly lesion on ear/forehead; Dx? → actinic keratosis
- Above patient with ulcerated lesion emerging from the red scaly lesion; Dx? → SCC → need to know actinic keratosis is precursor to SCC

- Risk factor for SCC apart from the sun → **USMLE is obsessed with immunodeficiency and smoking, even for cutaneous SCC**
- Biopsy of SCC? → keratin pearls + intercellular bridges
- Old scar or burn + new ulcerated lesion → answer = SCC (Marjolin ulcer) → chronically irritated area / burn / scar can lead to SCC (when I was in MS4 I saw an older woman with a Marjolin ulcer on her chin from a chickenpox scar she had since she was a kid)
- Ulcerated lesion on nose or pinna of ear + rolled/heaped-up edges → BCC
- Ulcerated lesion + telangiectasia visible → BCC
- Biopsy of BCC? → islands and nests of basophilic cells (dark purple)
- Blood transfusion + → fever + negative Coombs test; Dx? → febrile non-hemolytic transfusion reaction
- Most common blood transfusion reaction? → febrile non-hemolytic transfusion reaction
- Tx for febrile non-hemolytic transfusion reaction → **acetaminophen on the NBME, not prednisone**
- What causes febrile non-hemolytic transfusion reaction? → Abs against donor MHC antigens on RBCs or cytokines from leukocytes in the donor blood
- Blood transfusion + fever + chills + flank pain + hypotension → ABO mismatch (and positive Coombs)
Decreased hemoglobin + increased bilirubin 2-4 weeks after blood transfusion; Dx? → delayed transfusion reaction → caused by the presence of recipient “amnesic” antibodies (weird, but just memorize it)
- Blood transfusion + dyspnea + hypoxemia + bilateral pulmonary infiltrates; Dx? → TRALI (transfusion related acute lung injury)
- What causes TRALI? → donor Abs against recipient MHCs → activated neutrophils cause alveolar damage → most common cause of transfusion-associated death
- Dude moves into new apartment building and uses the hot tub a lot + has low oxygen sats + dyspnea + crackles at lung bases + no wheezing + low-grade fever → answer = **hot tub lung** (outrageous, but an answer on an NBME exam) → caused by hot tube fumes; not related to Pseudomonas (hot tub folliculitis) (weird factoid to end this pdf but we'll run with it)

- 72F + radical mastectomy 25 years ago + hard, raised purple lesions above the elbow; Dx? → lymphangiosarcoma (Stewart-Treves syndrome) → you don't have to agree that it's HY, but it's asked on the NBME → caused by chronic lymphatic insufficiency classically years after radical mastectomy.
- Neonate + spongy 1-cm red lesion on the chest; Dx? → strawberry hemangioma
- Strawberry hemangioma Tx? → don't treat; will grow slightly then regress spontaneously over a few years
- Neonate + large vascular lesion on the leg + thrombocytopenia; Dx? → Kasabach-Merritt syndrome (aka hemangioma with thrombocytopenia) → this is on the pediatric 2CK forms **three times** asked in different ways; students always say wtf and I have to explain that, yes, it's weird, but it's HY for some magical reason; this is not a strawberry hemangioma and requires surgical Tx.
- Neonate + large vascular lesion on the leg + thrombocytopenia; what is the cause of the thrombocytopenia? → answer = "platelet sequestration." I've memorized this from the NBMEs → similar to splenomegaly, which can cause thrombocytopenia from sequestration within the red pulp, the implication that the large vascular lesion of KMS is that platelets simply get caught within it.
- "Cherry red blood/lips" → CO poisoning
- "Brown blood" or "chocolate blood" → methemoglobinemia
- Kid with brown blood and they ask you the mechanism (answers are "upregulation of anti-proteinase 2" or "deficiency of cytochrome reductase B5") → answer = deficiency of cytochrome reductase B5; this is on the USMLE. I'm not fucking with you. And if you Wiki it, you'll see clear as day that they talk about congenital methemoglobinemia due to deficiency of cytochrome reductase B5.
- 22M + violaceous papules in a temporal distribution → answer = Sturge-Weber syndrome; student says "wtf? I thought that was associated with Port wine stain birthmark." Yeah, if we take a trip back to kindergarten, but you need to know it can present as **cutaneous papules** in a trigeminal nerve distribution.
- 44M alcoholic + winter + they show a pic of his feet and they're red; what electrolyte are we most worried about upon rewarming them → answer = hyperkalemia → alcoholics are notably susceptible to rhabdo (ultra HY on the USMLE) → rhabdo causes myoglobin release, which is nephrotoxic and can cause acute tubular necrosis (potassium goes up); even if the patient doesn't get full-blown rhabdo

with ATN, reperfusion injury can cause O₂ radical-mediated damage that induces cell lysis (increases K levels).

- 14M + ataxia + cognitive decline over a few months → answer = **glue**, **not** alcohol → no way a kid that young would get alcoholic cerebellar ataxia; this is on the NBME even if you find it stupid/weird.
- 16M found unconscious on floor in school bathroom + normal vitals + no eye findings + a little sluggish → answer = **butane (inhalant) toxicity** → caused by “dusters” / inhaling computer cleaner.
- Medial malleolus ulcer + hyperpigmentation of lower legs; Dx? → chronic venous insufficiency
- Punched-out ulcer on foot + intermittent claudication; Dx? → arterial insufficiency (peripheral vascular disease)
- What causes venous insufficiency? → valvular incompetence (most commonly familial), resulting in venous reflux + insufficiency.
- What causes arterial insufficiency → atherosclerosis (**diabetes, followed by smoking, are the two most acceleratory risk factors; hypertension is the most common risk factor**)
- How do you Dx venous insufficiency? → **duplex ultrasound** of the calves showing stasis and/or occlusive disease (the latter may result from venous insufficiency or cause it)
- How do you Dx arterial insufficiency? → USMLE always wants **ankle-brachial indices (ABI) first** → after this is done, the answer is **Doppler ultrasound** of the calves (duplex ultrasound is the answer for venous) **or arteriography**; both of these latter answers are correct; they will not give you both; it will be one or the other.
- Tx for venous insufficiency → compression stockings
- Tx for varicose veins → compression stockings
- Varicose veins and venous insufficiency same thing? → varicose veins are one of the mere presentations of venous insufficiency, so yes, patients with varicose veins have venous insufficiency.
- 47F has varicose veins + painful palpable cord by the ankle (is the treatment compression stockings or subcutaneous enoxaparin; both are listed) → answer = subcutaneous enoxaparin because this is superficial thrombophlebitis.
- Tx for arterial insufficiency → exercise regimen first, THEN cilostazol (phosphodiesterase 3 inhibitor)
- What must you do before starting the exercise regimen in the Tx of arterial insufficiency → **ECG stress test** to ascertain patient’s exercise tolerance.

- What if patient has abnormal baseline ECG (e.g., BBB) → do echo stress test instead.
- What if the patient can't exercise → do dobutamine-echo stress test
- What if the patient gets stable angina after merely walking up a flight of stairs → skip stress test and go straight to myocardial perfusion scan (myocardial scintigraphic assay); this is answer on the NBME.
- Patient has severe ischemia on stress test or myocardial perfusion scan → do coronary angiography → then do coronary artery bypass grafting if three-vessel disease, OR two-vessel disease + diabetic, OR single-vessel disease if it's the left main coronary.
- Patient with CVD is on various medications + has hyperkalemia; why? → ACEi, ARB, and spironolactone all can cause hyperkalemia.
- Patient with CVD is on various medications + hypokalemia; why? → furosemide (Loop diuretic)
- When do we start patients on furosemide? → to fluid unload (dyspnea in heart failure or peripheral edema)
- Patient is started on furosemide + still has fluid overload; what's the next diuretic to use → spironolactone (this is really HY on the USMLE and is on Steps 1 and 2CK NBMEs) → essentially furosemide causes increased K wasting, so we must give a potassium-sparing diuretic to balance the effect (spironolactone).
- What's the MOA of spironolactone → aldosterone receptor antagonist.
- Side-effects of spironolactone → hyperkalemia; gynecomastia.
- When do we give patients spironolactone apart from as a step-up from Loops? → added onto heart failure management after a patient is already on ACEi (or ARB) + beta-blocker. In other words, for heart failure: give ACEi (or ARB) first, then add beta-blocker, then add spironolactone.
- Major side-effects of beta-blockers → depression + sexual dysfunction (avoid in these patients)
- Major side-effect of naproxen → fluid retention (edema) due to increased renal retention of sodium.
- What is naproxen? → NSAID that the USMLE is obsessed with for some reason.
- Why might NSAIDs cause fluid retention / renal retention of sodium? → knocking out COX → decreased prostaglandin synthesis → decreased renal afferent arteriolar dilatation → decreased renal blood flow → PCT of kidney compensates for perceived low blood volume by increasing Na reabsorption → water follows sodium → edema.
- BUN/Cr ratio in someone with NSAID-induced interstitial nephropathy → >20 (pre-renal).

- What kind of vignette is a patient classically on naproxen? → osteoarthritis (OA).
- How do we treat OA? → weight loss (biggest risk factor is obesity), then acetaminophen, then NSAIDs
→ sometimes USMLE will mention naproxen being taken by OA patient to illustrate this common scenario of poor self-management → acetaminophen recommended before NSAIDs because the renal damage caused by NSAID use.
- What are the four beta-blockers that decrease mortality in heart failure? → Metoprolol XR (extended release) + carvedilol + nebivolol + bisoprolol → USMLE will never ask “extended-release”; they’ll just want metoprolol, but cardiologists will spasm out if you say regular metoprolol without specifying extended release; the idea being: we don’t give drugs like propranolol, atenolol, etc., for heart failure because they don’t improve mortality.
- When do we use “regular” metoprolol → classically first-line for atrial fibrillation rate control.
- When do we use atenolol → stage-fright
- When do we use propranolol → migraine prophylaxis, tachycardia in hyperthyroidism (decreases peripheral conversion of T4 to T3), esophageal varices prophylaxis, akathisia caused by anti-psychotics, hypertrophic cardiomyopathy to increase preload (HOCM and MVP are the two murmurs that get worse with low preload), essential tremor (AD familial tremor; patients self-medicate with alcohol, which decreases tremor; but propranolol can also be used for other tremors; social phobia (different from stage-fright)).
- Patient takes medication for muscle pain relief + gets wheezing (which should be avoided, acetaminophen or aspirin; both are listed) → answer = aspirin (aspirin-induced asthma)
- 27F + intermittent headaches + blurry vision; Dx? → optic neuritis (multiple sclerosis) → student says “why the headaches?” Yeah, I know. Weird. But it’s on the NBME. You need to know optic neuritis is HY in MS and means inflammation of cranial nerve II → presents as blurry vision, or change in color vision, or Marcus Gunn pupil (relative afferent pupillary defect)
- Most specific eye finding in MS → medial longitudinal fasciculus (MLF) syndrome → aka internuclear ophthalmoplegia (INO) → when you abduct to one side, you activate CN VI on that side, which requires the contralateral CN III to activate in order to adduct → the side that cannot adduct is the side that’s fucked up; the normal side will have nystagmus.
- Tx for acute flare of MS → IV steroids (oral is wrong and can make flares worse).

- Tx between flares of MS (the patient must be asymptomatic) → IFN-beta (interferon beta).
- Tx for spasticity in MS → baclofen.
- MOA of baclofen → GABA-B receptor agonist (USMLE loves baclofen).
- Dx of MS → choose MRI over CSF IgG oligoclonal bands if both are listed.
- Urinary incontinence in MS → urge incontinence (hyperactive detrusor / detrusor instability)
- 65F + unilateral temporal headache + blurry vision; Dx? → temporal arteritis
- Tx for TA → immediate IV methylprednisolone (IV steroids) to prevent blindness, **then** do temporal artery biopsy; **do not** choose biopsy before steroids.
- What other condition is TA associated with? → polymyalgia rheumatica (in fact, they're considered to be on the same disease spectrum, rather than as two inherently distinct conditions)
- 65F + unilateral temporal headache + muscle pain/stiffness → temporal arteritis + polymyalgia rheumatica
- Tx for PR if patient doesn't also have temporal arteritis → oral steroids are okay bc not an emergency.
- Polymyalgia rheumatica vs polymyositis → PR presents with stiffness/pain **generally without weakness**; polymyositis can present with pain, **but it also has proximal muscle weakness**. Both conditions can present with elevations of ESR and CRP, so these aren't reliable for Dx.
- Dx of PR → clinical; there's no specific test.
- Dx of polymyositis → same as with dermatomyositis, do anti-Jo1 and -Mi2 antibodies, then do confirmatory muscle biopsy.
- Oral + genital ulcers → Behcet syndrome
- Violaceous rash around the eyelids → heliotrope rash → Dx = dermatomyositis (don't confuse that with malar rash of SLE).
- Violaceous papules on knuckles + cracked/dry palms = dermatomyositis (Gottron papules + mechanics' hands).
- Rash around back of neck + top of back + adult with proximal muscle weakness (difficulty standing from chair unassisted) → shawl rash → dermatomyositis.
- Dx of dermatomyositis → anti-Jo1 or -Mi2 antibodies first → muscle biopsy confirmatory.
- Polymyositis = dermatomyositis but without the skin findings.

- USMLE wants you to know that in dermatomyositis, there's specifically an increased risk of what? → malignancy (non-Hodgkin lymphoma) → that being said, autoimmune diseases in general increase the risk of NHL → so if you have, e.g., patient with SLE with irregular ring-enhancing lesion on head CT, answer = primary CNS lymphoma, not toxoplasmosis.
- Tx for flare of polymyositis/dermatomyositis → oral corticosteroids.
- Antibodies in pemphigus vulgaris? → anti-desmoglein (anti-desmosome) → desmosomes enable adjacent cell-to-cell adhesion.
- Antibodies in bullous pemphigoid → anti-hemidesmosome → hemidesmosomes secure the dermis to the epidermal basal layer.
- Which one is worse, bullous pemphigoid or pemphigus vulgaris? → pemphigus vulgaris; why? → PV gets bullae on the skin that rupture with friction (Nikolsky sign) + scar → oral mucosal involvement is more prevalent in PV.
- What kind of immunofluorescence on biopsy in PV vs BV? → Linear in BV; net-like in PV.
- What else is associated with linear immunofluorescence on the USMLE? → Goodpasture syndrome (on biopsy of the kidney or alveoli).
- Tx for PV and BV → oral corticosteroids
- Mechanism for Goodpasture syndrome? → antibodies against type IV collagen → "2, 3, 4... 2, 3, 4... 2, 3, 4. The Goodpasture is marching in the field, 2, 3, 4!" → Type 2 hypersensitivity against the alpha-3 chains of type 4 collagen.
- Hematuria + hemoptysis + "head-itis" (mastoiditis, sinusitis, otitis, nasal septal perforation) → Wegener granulomatosis
- Annoying new name for Wegener → granulomatosis with polyangiitis
- Dx of Wegener → c-ANCA (anti-PR3; anti-proteinase 3)
- Asthma + eosinophilia → Churg-Strauss
- Annoying new name for CS → eosinophilic granulomatosis with polyangiitis
- Dx of CS → p-ANCA (anti-MPO; anti-myeloperoxidase)
- Hematuria in isolation + p-ANCA in serum → microscopic polyangiitis (MP)
- Severe renal disease in Wegener or Goodpasture or MP → rapidly progressive glomerulonephritis (crescentic)

- 44M + hematuria + hemoptysis → Goodpasture syndrome
- 44M + hematuria + hemopytisis + head-itis → Wegener
- What is polyarteritis nodosa → medium-vessel vasculitis characterized by immune complex deposition in vascular walls and fibrinoid necrosis
- Polyarteritis nodosa is associated with what infection? → 30% of patients are HepB positive
- What do you see on renal artery angiogram in PN → “beads on a string” (similar to fibromuscular dysplasia, although completely unrelated diseases).
- Which vessels are notably not affected in PN → pulmonary vessels (USMLE likes this detail).
- Tx for PN → oral corticosteroids
- 32F + arthritis + mouth ulcer + low platelets; Dx? → SLE
- Most common presentation finding in SLE → arthritis (>90%)
- Woman 20s-40s + arthritis + thrombocytopenia → SLE
- Woman 20s-40s + arthritis + mouth ulcer + circular skin lesions → SLE
- Malar rash + low RBCs + low WBCs + low platelets; mechanism for low cell lines? → increased peripheral destruction (antibodies against hematologic cells lines seen in SLE; isolated thrombocytopenia most common)
- Tx of SLE flare → steroids
- SLE + red urine; Dx? → lupus nephritis, more specifically, diffuse proliferative glomerulonephritis (DPGN)
- Histology of DPGN → wire looping capillary pattern
- Tx of lupus nephritis → mycophenolate mofetil
- Tx of discoid lupus → hydroxychloroquine
- Most specific Abs for SLE → anti-Smith (RNP), not anti-dsDNA
- Which Abs go up in acute SLE flares → anti-dsDNA (and C3 goes down)
- Drug-induced lupus Abs → anti-histone
- Drugs that cause DIL → Mom is HIPP → Minocycline, Hydralazine, INH, Procainamide, Penicillamine
- Viral infection + all three cell-lines are down → viral-induced aplastic anemia
- Viral-induced aplastic anemia; next best step in Dx? → bone marrow aspiration
- Viral-induced aplastic anemia; mechanism? → defective bone marrow production (contrast with SLE)

- 80F has catheter; how to best decrease infection risk in this patient (all answers listed sound reasonable) → correct answer = hand washing
- 17M has mononucleosis; how to best decrease risk of transmission? → answer = hand washing (“huh, I thought it was just kissing + sharing cups n stuff.” I agree with you. But the USMLE wants handwashing.
- 72M + intermittent claudication + absent distal pulses + Hx of coronary artery bypass grafting + high BP that’s been gradually increasing past two years; Dx? → renal artery stenosis
- 32F + high BP + high aldosterone/renin → fibromuscular dysplasia (tunica media proliferation in renal arteries) → this is **not** renal artery stenosis → if you say “renal artery stenosis,” that means atherosclerosis.
- Increased creatinine following medication administered to someone with renal artery stenosis; what was the drug? → ACEi or ARB
- Tx for RAS + FMD → initially medical therapy with cautious use of ACEi or ARB; definitive is renal angioplasty + stenting; FMD is not curable.
- Dx of malaria → thick + thin blood smears, **not** antibody titer for Plasmodium species
- Girl goes to Africa + is taking chloroquine prophylaxis → gets malaria anyway; why? Is the answer non-adherence or resistance to chloroquine? → answer = resistance to chloroquine
- What is the MOA of chloroquine? → inhibits Plasmodium heme polymerase.
- Which malaria type is the worst and why? → P. falciparum because it causes cerebral malaria.
- Fever cycles and malaria? → P. vivax/ovale have fever every 48 hours; P. malariae every 72 hours; P. falciparum causes sporadic/unpredictable fever.
- Which drug is often given to people for malaria prophylaxis who go to chloroquine-resistant areas? → mefloquine
- Girl goes to Africa + gets malaria + she is then treated after the fact with atovaquone + proguanil and the presentation subsides; then one month later she has malaria again; why? → answer = reactivation of non-erythrocytic form of organism” → she has P. vivax or P. ovale → cause hypnozoites which are an intra-hepatic form of the disease.
- Question literally asks you point-blank why a patient is given primaquine → answer = “primaquine kills hypnozoites” or “kills extra-erythrocytic forms.”

- Why does sickle cell confer resistance to malaria → decreased RBC lifespan (malaria needs normal RBC lifespan to complete life cycle)
- Travel + bloody diarrhea + RUQ pain; Dx? → liver abscess due to *Entamoeba histolytica*
- How do you Tx the liver abscess? → answer = percutaneous drainage **BEFORE** antibiotics
- Abx for *E. histolytica*? → metronidazole + iodoquinol (latter kills intraluminal parasite); paromomycin may also be given.
- Watery diarrhea in immunocompromised patient → *Cryptosporidium parvum*
- How is *Giardia* transmitted (is the answer “water-borne” or “fecal-oral”?); answer = water-borne
- Steatorrhea in guy who went swimming or scuba diving → *Giardia*
- Tx for *Giardia* → metronidazole
- Fever + periorbital edema + muscle aches + went to a BBQ; Dx? → *Trichinella spiralis* → this is a classic triad seen in trichinosis.
- How do you get trichinosis? → bear meat (yes, Alaska is still in the United States and people hunt polar bear) or pork (pork nematode, not cestode)
- What is nematode vs cestode vs trematode? → nematode is roundworm; cestode tapeworm; trematodes are flukes.
- Nematode from pork → *Trichinella spiralis*
- Cestode (tapeworm) from pork → *Taenia solium*
- What does *T. solium* cause? → cysticercosis (muscle cysts) or neurocysticercosis (brain cysts)
- “Swiss cheese appearance” of brain in someone who traveled abroad → neurocysticercosis
- Single cystic lesion seen on brain CT in someone who went to Mexico → neurocysticercosis
- Tx for cysticercosis / neurocysticercosis → praziquantel or albendazole (the USMLE will never give you both and make you choose between them; for anti-helminth drugs questions, the correct answer will be the only anti-helminth drug listed).
- Which helminth causes visceral larva migrans? → *Toxicara canis*
- Worm in the eye? → Loa Loa
- How do you get Loa Loa → deer, horse, or mango fly
- HIV patient with lobar pneumonia (is the answer PJP or *S. pneumoniae*?) → answer = *Strep pneumoniae* → PJP presents as bilateral interstitial infiltrates + groundglass appearance on CXR; *S. pneumoniae* is lobar →

sort of a trick Q similar to asbestos (i.e., bronchogenic carcinoma still more likely than mesothelioma in pt with Hx of asbestos exposure; well S. pneumo still more common than PJP in immunocompromised pts). The key though is the lobar vs bilateral presentation as mentioned above.

- Upper lobe nodular density in immunocompromised patient → Aspergilloma
- Dx of Aspergilloma → open lung biopsy
- 13F with irregular periods; next best step in Mx? → reexamine in one year (reassurance) → periods are typically abnormal in the first year following menarche
- 13F has never had a period + has suprapubic mass + nausea + vomiting; next best step in Mx? → answer = **do beta-hCG** → she's pregnant; this is HY. Correct, girls can get pregnant without ever having had a period → must rule out.
- 14F has massive unilateral breast mass + mom is freaking out bc her sister died of breast cancer → answer = follow-up in six months → **virginal breast hypertrophy** is normal during puberty.
- 15M has unilateral mass behind his nipple +/- tenderness of it → answer = reassurance → physiologic gynecomastia of puberty (higher androgens are aromatized to estrogens).
- Girl is Tanner stage 3; which of the following is true? → **answer = menarche is imminent** → USMLE asks this Q straight up and it's exceedingly HY and frequent.
- 17F + really pad period pain + physical exam is normal → answer = primary dysmenorrhea = prostaglandin hypersecretion (PGF2alpha) → give NSAIDs.
- 23F + really pad period pain + P/E shows nodularity of uterosacral ligaments → answer = endometriosis → do diagnostic laparoscopy.
- 14M is 3rd centile for height + bone age is less than chronologic age; Dx? → constitutional short stature (he'll catch up; his growth curve is just shifted to the right).
- 14M is 3rd centile for height; next best step in Dx? → ask for information about the parents' height trajectory → if they already say in the stem the parents are average height, answer = do bone age.
- 16F is Tanner stage II + wide neck + bone age is equal to chronologic age; Dx? → Turner syndrome → presents with genuine short stature (vignette will often say girl who's 4'11") + Tanner stage I or II + cystic hygroma (lymphatic insufficiency of neck; wide/webbed neck).
- Adult male is 4 feet tall + head and trunk are large in comparison to limbs; Dx? → achondroplasia

- Adult male is 4 feet tall + head and trunk proportional to limbs; Dx? → Laron dwarfism (growth hormone receptor defect → insensitivity to GH).
- Diffusely enlarged uterus + per vaginum bleeding → adenomyosis
- Globular uterus + per vaginum bleeding → leiomyomata uteri (uterine fibroids)
- 42M has surgery + two days later in hospital he has restlessness + tremulousness + tachycardia + diaphoresis; Dx? → delirium tremens (alcohol withdrawal)
- Tx for DT → long-acting benzo (diazepam or lorazepam or chlordiazepoxide) → USMLE likes chlordiazepoxide.
- 42M has surgery + two days later in hospital he has restlessness + tactile/visual hallucinations; Dx? → alcoholic hallucinosis → on the same spectrum as DT; Tx with long-acting benzo same as DT.
- When is buspirone the answer? → second-line Tx for generalized anxiety disorder (first-line is SSRI).
- MOA of buspirone → serotonin receptor agonist.
- Biochemical disturbance in Addison? → Low Na, high K, low pH, low bicarb
- Biochemical disturbance in Conn syndrome? → High Na, low K, high pH, high bicarb
- Pt has fatigue + normal Na, high K, low pH, low bicarb; Dx? → Addison (sodium can sometimes be normal in aldosterone derangement).
- 22F + BP of 160/110 on multiple office visits + MR angiography of renal vessels confirms diagnosis of fibromuscular dysplasia + labs show normal Na, normal K, normal pH, normal bicarb (Q is: what are her AT-II and aldosterone levels? Answers are up, down, no change for all the different combinations) → **answer = high AT-II + high aldosterone** → learning objective is: it's rare, but biochemistry can be completely normal in aldosterone derangement (Google it if you don't believe me) → [this is on the USMLE](#); if you get a vignette where they 1000% put in your face that a patient has high BP + a confirmed Dx of a cause of hyperaldosteronism, the answer is both AT-II and aldo are high.
- 2-year-old boy has writhing movements in his sleep + periventricular nodules seen on MRI of the head; what else would be seen in this pt? → answer = renal angiomyolipoma or cardiac rhabdomyoma → Dx = tuberous sclerosis (AD).
- Kid + heart tumor = cardiac rhabdomyoma until proven otherwise

- Adult + heart tumor = cardiac myxoma until proven otherwise (ball-in-valve tumor in the left atrium → causes a diastolic rumble that abates when patient is positioned in an unusual way, e.g., on his right side while leaning diagonally).
- 2-year-old boy has cardiac myxoma (correct, not rhabdomyoma) + perioral melanosis (sophisticated way of saying hyperpigmentation around the mouth/lips) + hyperthyroidism; Dx? → answer = **Carney complex** → [this is asked on the USMLE](#) → classically triad of cardiac myxoma + perioral melanosis + endocrine hypersecretion (classically bilateral pigmented zona fasciculata hyperplasia resulting Cushing syndrome, but can be hyperthyroidism or growth hormone).
- Biochemical disturbance in DKA → low Na, high serum K (hyperkalemia), low total body K, low bicarb, low pH, low CO₂.
- Biochemical disturbance in aspirin toxicity in first 20 minutes: normal O₂, low CO₂, high pH, normal bicarb → respiratory alkalosis only
- Biochemical disturbance in aspirin toxicity after 20 minutes: normal O₂, low CO₂, low pH, low bicarb → mixed metabolic acidosis-respiratory alkalosis → one of the 2CK pediatric NBME forms gives a teenage girl who ODed on aspirin 20 minutes ago + they list all of the different acid-base disturbances, and answer is mixed metabolic acidosis-respiratory alkalosis, **not** respiratory alkalosis. So whether you agree with it or not because you think the time frame is too early, I don't know what to tell you, it's the fucking answer on the NBME and everyone gets it wrong, including myself when I answered it. One thing I might point out however is that they said in this Q that the girl had lethargy, which I've noticed having gone thru different NBME Qs repeatedly as a tutor, can non-specifically imply metabolic acidosis → in other words, I've seen various Qs on surg, IM, and peds forms, etc., where there will be, e.g., lactic acidosis, and they'll mention lethargy. I have also seen lethargy in Addison disease Qs, but I would say **low cortisol causing chronic fatigue syndrome** is the more important association there.
- Patient has fever of 103F + Hb of 7 g/dL + platelet count of 50,000 + neutrophils are few; next best step in Mx? → immediate IV broad-spectrum antibiotics → fever + low neutrophils = febrile neutropenia, aka neutropenic fever; **this is a medical emergency** and means a patient has an infection but no way to fight it off → I have seen plenty of students select "give platelets" as the answer here, no idea why. It's really rare to transfuse platelets, but may be considered with counts

under 10-20k if there is spontaneous bleeding. We also tend to transfuse RBCs if under 7 g/dL, but if you get low neutrophils + fever in the same vignette, transfuse RBCs is wrong. I notice the “rule” of transfusing RBCs if Hb is 7 g/dL or lower causes students to get Qs wrong; think of it as a general propensity for transfusion, rather than as a mandatory answer for the Q.

- AV-nicking on fundoscopy → answer = hypertensive retinopathy
- Tx for hypertension? → if patient has pre-diabetes, diabetes, or any cardiovascular/cerebrovascular disease of any kind → **answer = ACEi or ARB first**. These agents decrease morbidity and mortality in these patient groups. If patient has none of the above (i.e., your typical fat American middle-age male who’s a little overweight but otherwise just has essential hypertension), the answer = **HCTZ or dihydropyridine CCB**. You might think that’s really weird (i.e., “why not just give an ACEi or ARB anyway to anyone if they’re good for morbidity/mortality?”), but the basis is: you’re not going to live to 120 just because you start taking a statin when it’s not indicated; well the same is true here: there’s no evidence of further improvement or morbidity/mortality in pts without the above risk factors if started on ACEi or ARB). This knowledge about how to Tx HTN is HY for 2CK.
- 32F + pedal + forearm edema after commencing anti-hypertensive agent; Dx? → answer = fluid retention / edema caused by dihydropyridine CCB (e.g., nifedipine) → really HY side-effect of d-CCBs!
- Side-effects of thiazides → hyperGLUC → hyperglycemia, -lipidemia, -uricemia, calcemia.
- Whom should you never give thiazides to? → prediabetics or diabetics → will push people into type II DM and make current DMs worse. One of the worst/frequent pharmacologic mistreatments. Also don’t give to pts with Hx of gout (bc of hyperuricemia risk).
- Diabetic pt on HCTZ for HTN → take them the fuck off the thiazide and put them on an ACEi or ARB.
- Important use of thiazide apart from HTN management in select patients → decreased risk of nephro- / ureterolithiasis (stones) because they cause hypocalciuria (and hence hypercalcemia).
- Delirium in patient on thiazide → think hypercalcemia → high Ca is HY USMLE cause of CNS dysfunction → “hypercalcemic crisis.”
- Renal issue + hypercalcemia; Dx? → nephrogenic diabetes insipidus → on the NBME.
- CNS disturbance due to an electrolyte problem → high or low sodium; high calcium
- Cardiac disturbance (arrhythmia) due to an electrolyte problem → high or low potassium or calcium

- Low calcium or potassium not responding to supplementation → check serum magnesium (low Mg can cause low Ca and K refractory to supplementation)
- Who gets low Mg → alcoholics (dietary deficiency; nothing malabsorptive or magic; they just drink too much and fill up on EtOH bc it's 7kcal/gram).
- Nutrition calorie counts: carbs + protein = 4kcal/g; fat = 9 kcal/g; EtOH = 7kcal/g.
- Tx for pulmonary hypertension → most patients respond to dihydropyridine CCBs (e.g., nifedipine).
- If patient fails the dCCB test, can try agents like bosentan or sildenafil.
- MOA of bosentan → endothelin-1 receptor antagonist
- 28F non-smoker has loud P2 + RVH; Dx? → primary pulmonary hypertension
- Which of the following is true in the above 28F? → answer = "increased vascular expression of endothelin 1." → if you know bosentan can treat, then inferring this is easy.
- VSD is repaired with a prosthetic patch; how will LV, RV, and LA pressures change? → answer = LV pressure goes up, RV pressure goes down, LA pressure goes down. → student says "the LA one is weird tho why is that?" Because if you decrease the LV → RV shunt, then there's less blood circulating back to the LA → decreased LA preload → decreased LA pressure.
- Kid is given over-the-counter med by his mom for a cold + gets mental status changes; Dx? → anticholinergic delirium caused by first-generation antihistamine (e.g., diphenhydramine, chlorpheniramine).
- 22M takes a drug + gets nystagmus + bellicosity (wants to fight) → **answer = PCP**.
- 22M takes a drug + gets mutism + has constricted pupils → answer = PCP. Fucking weird but it's on the psych NBME for 2CK. If you don't believe me, you can Google "pcp mutism constricted pupils."
- 2-year-old boy running + playing with 8-year-old sister + they were holding hands and he fell + now he holds arm pronated by his side; Dx? → **nursemaid's elbow** → radial head subluxation
- Tx for nursemaid's elbow → hyperpronation OR gentle supination (both are correct answers; only one will be listed).
- Kid falls on outstretched arm + pain over anatomical snuffbox; Dx? → scaphoid fracture
- Kid falls on outstretched arm + pain over anatomical snuffbox; next best step in Mx? → x-ray

- Kid falls on outstretched arm + pain over anatomical snuffbox + x-ray is negative; next best step in Mx? → **thumb-spica cast** → x-ray is often negative in scaphoid fracture; must cast to prevent scaphoid avascular necrosis → re-x-ray in 2-3 weeks.
- When is figure-of-8-strap the answer? → clavicular fracture
- What part of the clavicle gets fractured easiest? → middle-third
- First Tx for carpal tunnel syndrome in patient who can't stop offending activity (e.g., office worker) → **wrist splint first**; then **triamcinolone (steroid) injection into the carpal tunnel**; do not select anything surgical as it's always wrong on the USMLE; NSAIDs are a wrong answer and not proven to help
- Tx for cubital tunnel syndrome → elbow splint
- What is cubital tunnel syndrome → ulnar nerve entrapment at elbow → presents similarly to carpal tunnel syndrome but just in an ulnar distribution and involves the forearm.
- What is Guyon canal syndrome → ulnar nerve entrapment at the wrist → **hook of hamate fracture** or chronic handle bar impaction in avid cyclists.
- Most likely organism causing impetigo → **S. aureus now exceeds Group A Strep** for non-bullous ("regular") impetigo; for bullous, S. aureus has always exceeded S. pyogenes.
- Tx of impetigo → topical mupirocin
- Golden crusty lesions around the mouth in school-age child → impetigo, not HSV.
- 32F + sharply demarcated fiery red lesion extending from the knee to ankle + fever of 101F → answer = **erysipelas** → a Dx students never remember well → not as bad as cellulitis → erysipelas is infection of superficial dermis +/- dermal lymphatics, whereas cellulitis is hypodermis; the superficial nature of erysipelas gives it a well-demarcated, fiery appearance, whereas cellulitis is more diffuse and pink.
- Most common organism for erysipelas? → Group A Strep far exceeds S. aureus (but do not neglect the latter).
- Most common organism for cellulitis? → S. aureus exceeds Group A Strep.
- Treatment for erysipelas + cellulitis → oral dicloxacillin or oral cephalexin → both agents cover Staph + Strep; penicillin only covers Strep.
- Severe skin infection involving fascial planes + cutaneous crepitus; organism? → Clostridium perfringens causing necrotizing fasciitis (polymicrobial, but the C. perfringens causes the gas gangrene leading to cutaneous emphysema / crepitus).

- Tx for nec fasc → surgical debridement + IV broad-spectrum Abx with anaerobic coverage.
- Perineal gangrene in 50M diabetic → Fournier gangrene → do surgical debridement.
- 17M comes to emergency with cellulitis + getting worse + holding amoxicillin canister he got from GP;
Dx? → improper Abx treatment; should have received oral dicloxacillin or oral cephalexin outpatient
→ cellulitis must have been caused by Staph not Strep.
- Above 17M; what do you do? → Stat dose of IV flucloxacillin or IV cephazolin (inpatient equivalents of oral dicloxacillin + oral cephalexin).
- Why doesn't amoxicillin or penicillin cover Staph? → Most community Staph (not MRSA; just MSSA) produces beta-lactamase, so much give beta-lactamase-resistant beta-lactam (diclox and fluclox are steric; drugs like nafcillin and oxacillin are typically used for osteomyelitis; 6 weeks nafcillin is classic for confirmed MSSA endocarditis).
- Renal issue + beta-lactam or cephalosporin → interstitial nephropathy (aka tubulointerstitial nephritis) → WBCs on dipstick (eosinophils on Homer-Wright staining). Stress incontinence → weakened pelvic floor muscles resulting in loss of urine with increased abdominal pressure (coughing, sneezing, laughing) → Hx of multiple pregnancies classic, but often too easy of a descriptor and they won't say that → they'll say there's "downward movement of the vesicourethral junction with coughing"; next best step in Mx? → pelvic floor (Kegel) exercises → if insufficient, do mid-urethral sling; **do not** give medications for stress incontinence (HY!).
- USMLE might ask you which muscle is **not** strengthened by Kegel exercises → student then proceeds to have two thoughts: 1) "wtf, I'm supposed to know Kegel exercises at that high level of detail?" and 2) couldn't *any* muscle not be strengthened by Kegel exercises; I mean, the deltoid wouldn't be for instance." → **answer to this Q = internal anal sphincter** → even if you have zero clue about Kegel exercises, bear in mind **internal sphincters (urethral + anal) are under sympathetic control** → **you can't voluntarily strengthen a muscle not under somatic (voluntary) control**; in case you're curious though, Kegel strengthens levator ani (which comprises pubococcygeus, puborectalis, and iliococcygeus).
- Urge incontinence → answer = "hyperactive detrusor," or "detrusor instability" → needs to run to the bathroom when sticking a key in the front door; needs to run to bathroom when opening car door; answer in multiple sclerosis + menopause (part of vasomotor Sx); can be idiopathic; answer = give

oxybutynin (anti-muscarinic) or mirabegron (beta-3 agonist); **once again, do not give these drugs in stress incontinence.**

- Overflow incontinence → answer in diabetes and BPH → neurogenic bladder caused by myelin damage from sorbitol (glucose enters myelin, causing osmotic damage); in BPH, merely due to outlet obstruction → leads to detrusor burnout; **in overflow incontinence, postvoid volume is high (i.e., 300-400 mL in USMLE Qs)**; normal should be <50-75 mL; for diabetic bladder, answer = bethanechol (muscarinic agonist); for BPH, **insert catheter first always.**
- 72M + drooping of left side of face + decreased muscle strength and increased tendon reflexes of both left upper and lower extremities + Babinski on left + intact sensation; what's the most likely explanation for this patient's condition? → answer = lacunar infarct of internal capsule; produces "pure motor" stroke in most cases of posterior capsule infarct; thalamic stroke produces "pure sensory" effects; lacunar infarcts are usually due to Hx of HTN causes lipohyalinosis of lenticulostriate arteries.
- 24M + experiment glucose injected IV in two different scenarios: 1) when food is simultaneously consumed orally, and 2) when no food is simultaneously consumed; experiment shows that glucose is cleared faster from circulation when food is concurrently consumed orally; Q asks, which hormone is responsible for these findings? → answer = glucose-dependent insulintropic peptide (GIP); secreted in response to oral consumption of macronutrients (i.e., carbs, fats, protein); causes insulin secretion; in other words, insulin goes up more when food is consumed orally vs merely received parenterally → faster clearance of plasma glucose.
- 24M + receives 50g of glucose IV vs 50g of glucose orally; insulin goes up more when glucose consumed orally; why? → answer = glucose-dependent insulintropic peptide → greater insulin secretion.
- 6F + finds open bottle of aspirin; which of the following findings in the patient best suggests the dose consumed was toxic? → answer = increased respiratory rate; aspirin causes respiratory alkalosis acutely due to upregulation of respiratory centers (high pH, low CO₂, no change bicarb [too acute to change]); after roughly 20 minutes, a mixed metabolic acidosis-respiratory alkalosis is seen (low pH, low CO₂; low bicarb); the low bicarb **is not** compensation for the acute respiratory alkalosis; it is merely convenient that the salicylic acid itself is an acid and drops the bicarb; tachypnea is seen

acutely as first sign (observed by healthcare practitioner); tinnitus can be reported as first symptom (patient-reported finding); Tx with sodium bicarb → increased excretion of aspirin via urinary alkalinization.

- 30M + shooting groin pain + increased blood pressure + mother had surgery for thyroid cancer; what's most likely to establish the cause of the patient's HTN? → answer = urinary metanephrines; diagnosis is MEN 2A → pheochromocytoma + medullary thyroid carcinoma + primary hyperparathyroidism; Tx pheo with phenoxybenzamine (irreversible alpha blocker); shooting groin pain is urolithiasis secondary to hypercalcemia; medullary thyroid cancer causes increased serum calcitonin. For quick comparison, MEN 1 → pancreatic tumor, pituitary tumor, primary hyperparathyroidism; MEN 2B → pheochromocytoma + medullary thyroid carcinoma + mucosal neuromas + Marfanoid body habitus.
- Neonate + strange hereditary disease + mutation analysis shows homozygous gene deletion; what's the most likely inheritance pattern? → answer = autosomal recessive; some students get caught up by saying, "Wait, we're supposed to know the inheritance pattern of this weird disease?" No. It's the fact that they say *homozygous* deletion, without mentioning that either parent has pathology, that implies the condition is autosomal recessive.
- Patient takes nedocromil for seasonal allergies; what's the MOA of this drug? → answer = blocks release of autacoids from cellular storage; student says wtf?; mast cell stabilizers like nedocromil and cromolyn sodium prevent the release of histamine, which acts as an autacoid, which means it's a biologic molecule that acts as a local hormone (i.e., acts near site of synthesis).
- 84F + unilateral hydronephrosis caused by ureteral compression by a vascular structure; what's the structure → answer = ipsilateral common iliac artery; can compress ureter leading to hydronephrosis; if the Q tells you the patient has cancer causing unilateral hydronephrosis, choose ovarian cancer impinging on ureter; if Q tells you patient has bilateral hydronephrosis due to cancer, choose cervical cancer (usually younger patient).
- 54M + progressive shortness of breath for four months + ascites + edema of lower extremities + bilateral pleural effusions + ejection fraction of 55%; what's the mechanism for this patient's increased fluid in the lungs? → answer = decreased plasma colloid osmotic pressure (decreased plasma oncotic pressure); this refers to either renal (nephrotic syndrome) or hepatic disease

(decreased production of albumin); wrong answer is “increased capillary hydrostatic pressure” because ejection fraction is normal (55-70); this is normally the answer for pulmonary edema from left heart failure; “increased vascular permeability” would be the correct answer in ARDS (bilateral pulmonary infiltrates), infection (i.e., pneumonia +/- sepsis), or pulmonary embolism (local inflammation).

- Neonate + persistent cyanosis + normal Hct + normal RBC morphology + CXR and echo show no abnormalities; diagnosis? → answer = methemoglobinemia due to deficiency of cytochrome reductase B5; methemoglobinemia can lead to cyanosis; USMLE asks for cytochrome reductase B5 deficiency as cause of congenital methemoglobinemia; can lead to persistent cyanosis; should be noted that nitric oxide used for pulmonary hypertension in neonates can cause methemoglobinemia (oxidizes ferrous iron to ferric iron); acrocyanosis is normal blueish tinge of extremities at birth in some neonates (treatment is place under warming lights and do tactile stimulation); Tx for methemoglobinemia in most cases is methylene blue + vitamin C.
- 40F + fibromuscular dysplasia + GFR is within normal range; what explains this latter finding? → answer = increased efferent arteriolar resistance; RAAS will upregulate in response to decreased renal blood flow → angiotensin II constricts efferent arterioles, causing increased filtration fraction, where GFR is held constant despite lower blood flow to kidney.
- 19F + external compression of left renal artery but has normal renal perfusion pressure; what explains this latter finding? → answer = decreased *afferent* arteriolar resistance; just happens to be the answer they give in this hypothetical scenario; if the afferent perfusion is decreased due to compression of the renal artery, the only way perfusion pressure can still be unchanged is if the smaller afferent arterioles distal to the renal artery dilate; slightly unusual Q considering the normal physiologic response to reduced renal perfusion is simply efferent arteriolar constriction via increased RAAS activation; but in this latter scenario, the result is maintenance of GFR *despite* reduced renal perfusion, rather than a maintenance of renal perfusion.
- 27M + from Pennsylvania + Hx of splenectomy + RBCs show intraerythrocytic rings; diagnosis? → answer = Babesia; causes Malaria-like hemolytic disorder in patients who've never left the United States; ring forms and Maltese crosses can be seen within RBCs; if the Q tells you the patient went to

Africa, choose malaria, not Babesia. But if the patient didn't leave the US, malaria is the **wrong** answer.

- How many kilocalories in one gram of fat, carbs, protein, and ethanol? → answer = 9 kcal/g of fat; 4 for both carbs and protein; 7 for ethanol; USMLE Q will give you some nutrition Q where you have to do math, and it will rely on you knowing this nutritional info to get the Q right.
- Q asks for the mechanism via which insulin acts; answer = tyrosine kinase (MAP); USMLE also wants you to know that insulin causes ↑ nuclear transcription, ↑ serine-threonine kinase activity, and ↓ ubiquitin-mediated proteolysis.
- Patient has infection + goes into septic shock; Q asks for what LPS binds to that causes shock; answer = Toll-like receptors; in endotoxic shock, the lipid A of lipopolysaccharide (LPS) binds to CD14 on macrophages (toll-like receptor 4; TLR-4), resulting in macrophages releasing cytokines, namely TNF- α and IL-1. Do not confuse endotoxic shock with toxic shock syndrome caused by *S. aureus*, where TSST toxin (superantigen) bridges MHC-II and TCR, causing the macrophage to release cytokines; if the Q mentions cotton nasal packing or tampons, choose the MHC-II + TCR combo, not CD14/TLR-4.
- 2F + missing superior left parathyroid gland; what's the embryologic defect? → answer = fourth pharyngeal pouch; fourth pouch = superior parathyroids; third pouch = thymus + inferior parathyroids; easiest student fuck-up = selecting arch instead of pouch; pouches = endoderm; arches = mesoderm; clefts/grooves = ectoderm; DiGeorge syndrome → aplasia of 3rd and 4th pharyngeal pouches, leading to hypocalcemia, T cell deficiency with absent thymic shadow, cleft lip/palate, and heart defects (tetralogy of Fallot; truncus arteriosus).
- 20F + recurrent Staph infections + deficiency of CD18; what mechanism best explains this condition? → answer = failure of emigration of phagocytes to inflamed tissues; leukocyte adhesion deficiency is caused by deficiency of LFA-1/CD18 integrin, which is required for diapedesis of leukocytes to sites of infection; result is recurrent infections (often Staph) with absent pus; delayed separation of umbilical cord is often omitted from Qs because it's too easy of a detail.
- 40F + develops AML after exposure to agent; what's the most likely agent? → answer = benzene. You need to know benzene exposure is associated with AML. Naphthylamine is associated with urothelial cancers (i.e., transitional cell carcinoma); vinyl chloride can cause angiosarcoma of the liver.

- 54F + treated with anti-platelet agent that prevents platelets from interacting with fibrinogen; what's the agent? → answer = abciximab → monoclonal antibody against glycoproteins IIb/IIIa on platelets; these glycoproteins carry out aggregation and are normally bridged by fibrinogen; abciximab is a fibrinogen analogue; don't confuse aggregation (platelets to each other) via GpIIb/IIIa with adhesion (platelets to endothelium) mediated by Gp Ib. Eptifibatide and tirofiban are lower yield drugs that also inhibit GpIIb/IIIa; abciximab is HY agent with this MOA; HY drugs that inhibit ADP2Y12 receptor on platelets are clopidogrel and prasugrel; ticagrelor and ticlopidine are lower yield drugs that antagonize ADP2Y12.
- Which of the following is both an anti-platelet agent and vasodilator? → answer = cilostazol; both cilostazol and dipyridamole inhibit platelet phosphodiesterase; cilostazol used for intermittent claudication *after* exercise regimen fails; dipyridamole-thallium is a type of pharmacologic stress test (answer on USMLE if patient needs AAA repair but perioperative MI risk needs to be assessed).
- 57M + asks physician why celecoxib increases risk of adverse cardiovascular events; answer = inhibits platelet prostaglandin synthesis without inhibiting thromboxane synthesis; celecoxib is selective COX2 inhibitor.
- 35F + started taking high-dose vitamins past few months as part of new dietary regimen + has cracked lips, rough/dry skin, and alopecia on scalp; these findings are due to excess of which vitamin? → answer = vitamin A → can cause desquamation, increased hepatic transaminases, dyslipidemia, and pseudotumor cerebri (increased intracranial pressure); teratogenic; must do pregnancy test before commencing isotretinoin for acne.
- 46M + alcoholic + Q shows you hypersegmented neutrophil; what's the vitamin deficiency? → answer = folate (B9); most common vitamin deficiency; B9 deficiency also the answer for history of tea and toast diet for 6 months, and anti-epileptic use (i.e., valproic acid, phenytoin, carbamazepine); B12 is the answer for veganism, strict vegetarianism, chronic gastritis, pernicious anemia, Hx of gastrectomy or ileectomy, Crohn disease, *D. latum* infection.
- 34F + receives phentolamine; what intracellular effect is expected? → answer = ↓ phospholipase C activity; phentolamine is α_1 antagonist; α_1 is coupled to a G-alpha-q G-protein. Agonism will ↑

phospholipase C activity, which will \uparrow IP3 and \uparrow DAG; therefore antagonism will \downarrow phospholipase C activity, \downarrow IP3, and \downarrow DAG.

- 17F + Hx of heavy menses + easy bruising + \downarrow Hb + normal platelets + normal PT + \uparrow PTT; what factor is she deficient in? \rightarrow answer = von Willebrand factor; vWF bridges Gplb on platelets to vascular endothelium; deficiency in vWD causes: \uparrow bleeding time, normal PT, and \uparrow PTT *about half the time*. Bleeding time is always elevated because the primary role of vWF is to ensure platelet adhesion; PTT is only increased about half the time because vWF's stabilization of factor VIII in plasma is a mere secondary/ancillary role. Plenty of NBME Qs will have normal PTT in vWD. Platelets can be normal or slightly decreased. Vignette of vWD will always give a mix of one platelet problem (easy bruising, petechiae, epistaxis) and one clotting factor problem (menorrhagia, excessive bleeding with tooth extraction). Hemarthrosis is a clotting factor problem but is seen more in hemophilia rather than vWD. vWD is AD; hemophilia A and B are XR.
- Q asks about which of the following is most likely to disturb Hardy-Weinberg equilibrium; answer = "appreciable rate of gene mutation"; H-W assumes: there is no appreciable rate of gene mutation; mating within a population occurs at random; the population is relatively large; there is no selection against a particular genotype; and there is no significant immigrant population.
- 43M + elevated fasting glucose + arthritis + cardiomegaly; what's the mechanism for this patient's condition? \rightarrow answer = increased intestinal absorption of iron; Dx = hemochromatosis; AR; chromosome 6; Fe can deposit in tail of pancreas, leading to diabetes; hemochromatosis and primary hyperparathyroidism are two HY causes of pseudogout (calcium pyrophosphate deposition disease); this will carry an osteoarthritis-like presentation (i.e., even with findings such as Heberden nodes), but the vignette will be hemochromatosis and primary hyperparathyroidism, so you know the Dx is pseudogout; Fe can deposit in the heart, leading to either dilated or restrictive cardiomyopathy; Fe can deposit in the hypothalamus and/or testes, causing infertility; "Bronze diabetes" = hyperpigmentation of the skin due to hemosiderin deposition \rightarrow e.g., patient with darkening of the skin of the forearms, increased fasting glucose, and infertility or arthritis; answer = "check serum iron and ferritin."

- 6M + hyperpigmentation around the lips + colonic polyps; what kind of polyps are they? → answer = hamartomatous; Dx = Peutz-Jeghers syndrome, characterized by perioral melanosis + hamartomatous colonic polyps.
- 26F + hyperpigmentation + BP of 100/60 + muscle weakness; what combination of sodium, potassium, and cortisol are expected in this patient? → answer = ↓ sodium, ↑ potassium, ↓ cortisol; Dx is Addison disease; Na is ↓ and K ↑ because aldosterone is ↓. Condition is often caused by antibodies against 21-hydroxylase, which is needed to synthesize both aldosterone and cortisol in the adrenal cortex.
- 80F + colonic diverticula; which part of the colon most likely has the diverticula? → answer = sigmoid colon.
- Q asks about what would be increased in third trimester of pregnancy; answer = “hepatic protein production”; in contrast, CO₂ is decreased (a mild respiratory alkalosis can be seen in pregnancy); pulmonary residual capacity is decreased because the diaphragm is pushed up; serum osmolality is decreased due to expansion of plasma volume, resulting in dilutional effects; systemic vascular resistance is decreased because the placental vessels add units to the “parallel circuit” of the systemic vasculature.
- 40F undergoing chemotherapy + has low leukocyte count; what drug will help this patient? → answer = pegfilgrastim (granulocyte colony-stimulating factor; G-CSF); will cause an increase in neutrophils.
- 27M + infertility + high serum testosterone + low serum LH and FSH; what’s the most likely cause of this patient’s infertility; answer = exogenous testosterone use; testosterone-secreting tumor could also theoretically be an answer, but only the former listed.
- 25M + has facial nerve and optic nerve on left damaged in car accident; why does he regenerate facial movement over time but not vision? → answer = optic nerve is myelinated by oligodendrocytes; oligodendrocyte-myelinated nerves of CNS have limited regenerative capacity compared to Schwann cell-myelinated nerves of the PNS; facial nerve is myelinated by Schwann cells.
- Drug is given that increases insulin release; what is the MOA of this drug? → answer = increases the ATP/ADP ratio; theoretically, many answers could make sense here; the point is: does the student know the mechanism for insulin release: ATP closes a K⁺ channel on the beta-islet cells → K⁺ builds up within the cell → depolarization → Ca²⁺ then influxes → causes release of insulin-containing

vesicles from beta cell; in other words, if a drug increases the ATP/ADP ratio within the beta islet cell, then theoretically that would facilitate insulin release. In real life, sulfonylureas (e.g., glipizide) function to close the ATP-gated K⁺ channel without the need for ATP.

- 46M + esophageal varices; which vein is most likely to have increased blood flow? → answer = left gastric vein; ↑ portal venous pressure causes backup to left gastric vein, which backs up to esophageal veins.
- 74M + lesion on cheek showing neoplastic cells with dense pigment granules; what's the diagnosis? → answer = melanoma. Sounds like pigmented BCC, but USMLE wants melanoma for this description. BCC histologically can be described as having islands and nests of basophilic cells; squamous cell carcinoma has keratin pearls and intercellular bridges.
- Woman gets toxoplasmosis but cats isn't listed as an answer; where did she get it from? → answer = pork; can also be written as just simply "delicatessen meats"; both answers on offline NBMEs.
- Biostats Q asks about what increasing the # of participants in a study would result in; answer = decreased standard error of the mean; $SEM = SD / (\text{square root of the \# of samples})$; so if samples increase, then the denominator increases, and SEM decreases. Increasing # of samples will also increase power and decrease beta error (false-negative error).
- 50F + weight loss + progressive shortness of breath + CXR shows pleural-based mass encasing the lungs; what kind of cells are this patient's malignant cells derived from? → answer = mesothelial cells; mesothelioma will classically present with pleural and/or supradiaphragmatic plaques; if shown a gross specimen, mesothelioma will appear to surround the lungs circumferentially, rather than appearing as an isolated mass.
- 30F + last menstrual period 8 weeks ago + USS shows no obvious fetus or gestational sac + curettage shows trophoblastic proliferation; what will chromosomal analysis of this tissue show? → answer = 46XX; Dx = complete mole; empty egg fertilized by one sperm that then duplicates (i.e., genetic material is only of paternal origin); complete mole has *no* fetal parts; partial mole carries 67 chromosomal karyotype → one egg fertilized by two sperm; fetal parts present on USS.
- Pic is shown of cavitating lung cancer; what's the diagnosis? → answer = squamous cell carcinoma; can present with cavitary/cavitating lesion.

- 35F + menorrhagia + deep/hoarse voice + delayed tendon reflexes + large, globular heart with crackles at lung bases + low Hct + low MCV; next best step? → answer = check serum TSH; patient likely has Hashimoto (hypothyroidism); can cause menorrhagia, reduced reflexes, and cardiomyopathy. Anemia in this case is likely IDA due to heavy periods (although anemia of chronic disease does indeed present with low MCV on many NBME Qs); other HY findings for hypothyroidism are hypothyroid myopathy (↑ serum CK), ↑ LDL cholesterol, ↑ hepatic transaminases, and low mood; findings such as constipation, cold intolerance, brittle hair, and doughy skin are often omitted from Qs because they're too easy.
- Biostats Q where researchers conclude there's no increased risk of cancer in one study group vs another, with a p value of 0.02; what does this p value indicate? → answer = probability of accepting the null hypothesis when it's false. This study concluded that there was no difference between the groups, so they are saying there's a 2% chance they fucked up, where there really was a difference but they just didn't catch it (i.e., beta error, or false-negative error); a p value given for a study conclusion, in general, = the chance your conclusion is wrong; so if you get another biostats Q where they say, yes, there was a difference between two drugs, with p value of 0.01, the interpretation is: there's a 1% chance we fucked up and there really was no difference between these drugs (i.e., a 1% chance we rejected the null hypothesis when it was true).
- Study finds high sugar consumption causes prostate cancer, with p value of 0.07; what does this p value indicate the probability of? → answer = chance of rejecting a true null hypothesis. In other words, a true null hypothesis means there really is no increased risk of prostate cancer caused by sugar. But because the study said there's a difference, they rejected the null hypothesis. And the p value of 0.07 means they're saying there's a 7% chance they acknowledge they fucked up, where they said there was increased risk of cancer even though in truth there isn't.
- Q asks which of the following agents is an NMDA receptor antagonist; answer = ketamine; NMDA receptors are a type of glutamate receptor; ketamine is an NMDA glutamate receptor antagonist.
- Q asks which of the following will occur as a result of giving bortezomib; answer = decreased activation of CD8+ T cells; bortezomib is a proteasome inhibitor that causes decreased MHC I expression.

- 25M + motorcycle accident + now cannot dorsiflex left foot but eversion intact; Q asks which nerve is fucked up; answer = deep peroneal (fibular) nerve; **d** deep does **d**orsiflexion and sensation of the webbing between the first and second toes; superficial peroneal (fibular) nerve does eversion + sensation over most of the dorsum of the foot; common peroneal nerve injury would result in both loss of dorsiflexion and eversion; tibial nerve injury results in loss of plantar flexion and sensation over sole of the foot.
- 21F + vesicular, painful rash across left flank + pic shows you multinucleated giant cells; what's the most likely pathogen this patient should be screened for? → answer = HIV; only answer listed that makes sense, as VZV not listed; young patient with shingles (herpes zoster; VZV); immunosuppression in young patient resulting in shingles could reflect HIV infection.
- 25M + 3-day Hx of paresthesias of the legs + difficulty swallowing + diminished tendon reflexes + CSF shows protein of 70 mg/dL and cell count of 5/uL; what's the mechanism for this patient's condition? → answer = "destruction of myelin and endoneurial lymphocytic infiltrates"; USMLE wants you to know this description of Guillain-Barre; CSF findings are albuminocytologic dissociation (increased protein but normal cells).
- Q asks for which type of receptor agonism is associated with pain and itching; answer = H1 agonism; second generation H1 blockers such as loratadine can be used for anti-allergy effects; first generation agents such as diphenhydramine and chlorpheniramine have strong anti-cholinergic side-effects and can actually be used, for this reason, as treatment for acute dystonia and motion sickness.
- 30M + sensory nerve injury in bar fight; Q asks what's the rate-limiting step in reestablishing normal sensation in this patient; answer = slow anterograde axonal transport; Wallerian degeneration results in breakdown of axonal skeleton and myelin sheath distal to site of nerve injury; nerve regrows anterograde from site of lesion at 1mm/day; slow anterograde transport / regeneration of nerve becomes rate-limiting factor in restoration of function.
- 25M + rash on palms and soles + receives antibiotic Tx with drug he has received in the past; following current Tx, now has fever, tachycardia, and tachypnea; what's the most likely diagnosis? → answer = Jarisch-Herxheimer reaction; answer can also be written as "reaction to lysis of spirochetes"; patient has secondary syphilis (*Treponema pallidum*), as indicated by the palms/soles rash; Tx is with penicillin G; lysis of spirochetes can cause anaphylaxis-like immune response known as J-H reaction.

- 30F + rheumatoid arthritis + currently being managed with infliximab but has not improved; Q asks for which immune mediator is most likely contributing to symptoms; answer = IL-1. Infliximab is a monoclonal antibody against soluble TNF α (not TNF α receptor); even though TNF α plays a role in rheumatoid arthritis, we know TNF α is not the answer here because the patient is already on a med for it; IL-1 and IL-6 are cytokines known to cause inflammation in RA; tocilizumab is a monoclonal antibody against IL-6 receptor that can be used for advanced RA.
 - Normal Tx for RA is two-armed: symptoms and DMARDs (disease-modifying anti-rheumatic drugs).
 - For Sx: USMLE wants NSAIDs followed by steroids; these do **not** slow disease progression.
 - For slowing disease progression, the first-line DMARD is almost always methotrexate. If this fails or patient has contraindications to it (i.e., pulmonary or hepatic disease), use an anti-TNF α drug.
- Simple Q asking the function of Sertoli cells; answer = produces aromatase.
 - Sertoli cells are stimulated by FSH and produce androgen-binding protein, aromatase, and inhibin. Anti-Mullerian factor is also made by Sertoli cells in fetus.
 - Leydig cells are stimulated by LH and produce androgens.
 - The androgens produced by Leydig cells are converted to estrogens by the aromatase produced by Sertoli cells.
 - Androgen-binding protein binds testosterone locally and keeps concentrations high in the seminiferous tubules, enabling spermatogenesis. Do not confuse ABP with sex-hormone-binding globulin, which is produced by the liver and binds androgens and estrogens for transport around the blood.
 - Leydig cells in males = theca interna cells in females.
 - Sertoli cells in males = granulosa cells in females.
 - Sertoli-Leydig cell tumor (seen in females as well, despite the name) produces androgens → leads to hirsutism/virilization; can also cause gynecomastia because ↑ androgens can be aromatized to estrogens.

- Granulosa cell tumors classically present on USMLE as endometrial hyperplasia due to unopposed / higher estrogen levels → can cause endometrial cancer (bleeding per vaginum).
- 20M + both common carotids are compressed externally for 10 seconds; what effect will this have on alveolar ventilation, venous tone, arterial tone, and blood pressure; answer = all are ↑.
 - If blood flow is ↓ to the carotid sinus (area just superior to bifurcation of common carotid bilaterally) → ↓ stretch of baroreceptors → ↓ CN IX (glossopharyngeal) afferent firing to solitary nucleus of medulla (**not** ↑ firing, because the rate of firing is stretch-dependent) → ↓ efferent CN X (vagus; parasympathetic) + ↑ efferent sympathetic firing to cardiac nodal tissue → ↑ heart rate.
 - ↑ sympathetic efferent firing also causes ↑ arteriolar and venous vasoconstriction via α_1 agonism (↑ SVR → ↑ BP) + ↑ bronchodilation and respiratory rate via β_2 agonism.
- 39M + bilateral renal enlargement + high blood pressure + father died from subarachnoid hemorrhage; this patient most likely has a gene mutation in which protein? → answer = polycystin; diagnosis is ADPKD; high blood pressure is from cysts impinging on the renal microvasculature leading to surges in RAAS.
- 52M + 3-month-Hx of burning in esophagus + Hx of diabetes + ↓ pin-prick discrimination up to ankles + HbA1c of 9.6%; what's the MOA of the most appropriate pharmacologic therapy? → answer = antagonism of D2 receptors; drug is metoclopramide; Dx is diabetic gastroparesis; metoclopramide is both a pro-kinetic and anti-emetic.
 - In contrast, if vignette is simply 42M + GERD-like presentation + no mention of poor diabetic control, answer is "trial of PPIs" or "trial of H2 blockers" (I've seen both as correct answers, but if you're forced to choose between the two, always choose PPIs) for GERD.
- 30F + cuts finger on paper; moments after the cut, the bleeding stops; which of the following is the mechanism for the quick cessation of blood loss? → answer = localized secretion of endothelin; sounds slightly unusual, as endothelin is notably increased in pulmonary vascular resistance, but it acts peripherally as well.

- Endothelin is \uparrow in pulmonary hypertension, cor pulmonale, and congestive heart failure (including isolated left heart failure); essentially any cause of increased pulmonary pressure leads to \uparrow compensatory endothelin release (to restrict the increased blood flow).
- 28M + renal failure + hematuria + hearing loss; what's the mechanism for this patient's disease? \rightarrow answer = mutation in type IV collagen (Alport syndrome, X-linked); wrong answer is antibodies against type IV collagen (Goodpasture); Alport \rightarrow hematuria in a male + ear and/or eye problem; Goodpasture \rightarrow male 20s-40s with hematuria and hemoptysis.
- 19F + alkaline urine + renal tract calculi; which organism is most likely responsible? \rightarrow answer = Proteus; other correct answers could be Klebsiella or Serratia; struvite (ammonium magnesium phosphate) stones form in alkaline urine secondary to UTIs caused by urease-positive organisms.
- 62F + high Hb + high WBCs + high platelets + pO₂ 93%; what combination of EPO and arterial O₂ blood content is most likely in this patient? \rightarrow answer = \downarrow EPO + normal arterial O₂ content; diagnosis is polycythemia vera (JAK2 mutation), which is a bone marrow overproduction of the different cell lines; the high primary RBC production by the bone marrow suppresses EPO production by the kidney; WBCs and/or platelets will also be increased. In contrast, in secondary polycythemia caused by lung disease (\uparrow EPO due to \downarrow O₂) or renal cell carcinoma (\uparrow EPO production by cancer), only RBCs are high. High hemoglobin (>17.5 g/dL) is seen + Hb-O₂ saturation that is at the lower end of normal (93% is minimally acceptable); arterial O₂ content = pO₂ (dissolved O₂) + Hb-O₂ (amount bound to Hb); since Hb is high, less is saturated, but the amount of O₂ in the blood (content) is still the same because there is no lung disease, and Hb can still bind O₂ without a problem. Tx for polycythemia vera is serial phlebotomy.
- What is the role of I κ B in relation to NF κ B? \rightarrow answer = "releases NF κ B after undergoing phosphorylation"; USMLE also wants you to know that corticosteroids \downarrow NF κ B signaling in leukocytes.
- Newborn + chorioretinitis + cataracts + microcephaly + no other info; Dx in the neonate? \rightarrow answer = CMV; congenital Toxo always = triad of chorioretinitis + hydrocephalus + intracranial calcifications; so if you do not get this exact latter triad, you can eliminate congenital Toxo. Congenital CMV tends to have a mix of non-specific findings, e.g., deafness, chorioretinitis, intracranial calcifications. Congenital rubella will have PDA; congenital syphilis will have tooth abnormalities (Hutchinson), and

often saddle nose and/or Saber shins. Congenital VZV will have zig-zag skin lesions, limb abnormalities, and microphthalmia.

- 14M + temp 103F + WBCs 25,000 with neutrophil shift; what's the mechanism for the high leukocytes in this patient's blood? → answer = accelerated release of leukocytes from bone marrow postmitotic reserve pool; diagnosis is leukemoid reaction, which means leukocytosis in the setting of infection; leukocyte ALP is high; smear can show neutrophilia (i.e., a smear showing just, e.g., 8 neutrophils).
- Q asks what the anticodon sequence of tRNA does; answer = selection of specific mRNA for ribosomal binding; tRNA anticodon is a 5'→3' sequence that is complimentary to the codons of mRNA; when a codon of an mRNA codes for a specific amino acid, this is because a corresponding (and complimentary) tRNA binds to it via its anticodon site. The tRNA has an amino acid bound at its acceptor stem. The tRNAs then transfer amino acids to the growing peptide strand at the ribosomes during protein synthesis.
- 15M + skiing accident + tachycardia + tachypnea + BP 98/72 + decreased breath sounds on right + CXR shows decreased lung markings on one side and large, black pleural space; Dx? → answer = tension pneumothorax; blood pressure can be low or low-normal; tension pneumothorax is a pneumothorax in which hemodynamic decompensation occurs (i.e., low BP); in this patient, although BP is technically low-normal, this is only because the HR is increased to compensate, and the patient will likely continue to decompensate. Mechanism for low BP in tension pneumothorax is compression of venous structures returning blood to right atrium; Q need not mention contralateral tracheal deviation; breath sounds will be decreased on affected side because air does not move in and out through the pleural space; Tx is needle decompression followed by chest tube connected to underwater apparatus.
- 36M + stab wound to chest + low BP + JVD + systolic BP drops 12 mmHg on inspiration; Dx? → answer = cardiac tamponade; Beck triad for cardiac tamponade = hypotension, JVD, muffled heart sounds; Q need not mention all three. Pulsus paradoxus, with drop of systolic BP >10 mmHg with inspiration is classically seen in tamponade; tamponade is simply a pericardial effusion + hemodynamic decompensation (i.e., low BP, or low-normal BP with high HR to compensate); ECG shows electrical alternans (alternating QRS amplitudes due to blood moving within the pericardial sac, causing fluctuation in distance between the leads); ECG will show same finding in simple pericardial effusion

that is not tamponade; Tx is echo to confirm followed by pericardiocentesis or pericardial window.

Factor that is most important for tamponade development is acuteness of blood accumulation, not volume – i.e., stab wound, or LV free-wall rupture post-MI, can lead to small volume of blood accumulating quickly in pericardial sac, leading to tamponade, whereas, e.g., lymphatic obstruction from lymphoma could cause slow-accumulating, high-volume chylous effusion over many months that does not cause tamponade.

- Hemothorax is contrasted with tamponade in that in the former, there are flattened neck veins, whereas in tamponade, there's JVD. This is how to distinguish if they don't mention the CXR or decreased unilateral breath sounds for hemothorax.
- 42F + in hospital for surgery two days ago + shortness of breath + HR 92 + ECG shows no abnormalities; the medication she needs has what MOA? → answer = activation of anti-thrombin; heparin is drug given; diagnosis is pulmonary embolism; sinus tachycardia is most common finding on ECG (normal ECG + ↑ HR = sinus tachycardia); after heparin, do spiral CT of chest for diagnosis; do V/Q scan first in pregnant women.
- 29M + lancinating/stabbing pain in cheek lasting several seconds + happens spontaneously; Q asks location of problem; answer = pons; unusual answer, since trigeminal neuralgia is a peripheral mechanism, but CN V comes from pons; answer can also be "microvascular compression of CN V"; no acute Tx since the Sx subside so quickly; prophylaxis is carbamazepine.
 - Do not confuse trigeminal neuralgia of the V1 distribution with cluster headache; the latter will occur usually during sleep and will last up to half hour; details such as lacrimation and rhinorrhea are HY but too easy and often omitted from Qs; Q can mention pupillary changes during cluster headache; Tx = 100% oxygen; prophylaxis is verapamil (not propranolol).
 - Migraine prophylaxis on USMLE = propranolol (sometimes just written as beta blockade); Tx is NSAIDs followed by triptans (serotonin receptor agonists).
- 23F + relaxing after coming back from a run; which of the following describes her changes in diastole and systole as her heart rate returns to normal? → answer = diastole increases more than systole; the Q can also be asked as the inverse: that is, as HR increases, diastole shortens more than systole; the learning point is that the slower the heart rate, the greater the proportion of time spent in diastole.

- 40F + goes for run; which of the following regarding diastole and systole represent her coronary artery filling pressure at rest vs while running? → answer = at rest: diastole > systole; while running: diastole > systole; answer is the same for both; the coronary arteries fill during diastole irrespective of how fast the HR is.
- 50M + severe upper back pain + 3/6 holo-diastolic murmur loudest after S2; Dx? → answer = aortic dissection; classically pain radiating back between the scapulae; retrograde propagation of the dissection can cause aortic root dilation with aortic regurgitation (decrecendo holo-diastolic murmur); CXR shows widening of the mediastinum; give labetalol to decrease shearing forces; increased risk in connective tissue disorders such as Marfan and Ehlers-Danlos; greatest risk factors are hypertension and cocaine use.
- 19M + comes to physician with chest pain after night of heavy partying + walks through the door bent over at the waist; next best step in diagnosis? → answer = ECG showing diffuse ST-elevations; diagnosis is pericarditis; pain is lessened when leaning forward + worsened when leaning back; ST-elevations will be seen in most leads, as opposed to 3-4 contiguous leads, as with MI; cocaine is risk factor for serous pericarditis; Tx with NSAIDs, corticosteroids, and colchicine.
- 37F + rheumatoid arthritis + PR-depressions and ST-elevations seen in many leads on ECG; diagnosis? → answer = pericarditis; common in autoimmune diseases such as RA; PR-depressions are highly specific for pericarditis but not common; diffuse ST-elevations seen in all cases on USMLE if they mention ECG findings.
- 34F + severe chest pain + worse when reaching behind her back and above her head; diagnosis? → answer = costochondritis → MSK because changes with position (pericarditis only exception when cardiac).
- 34F + chest pain that does not change with position + chest pain worse with palpation; diagnosis? → answer = costochondritis; even though it doesn't change with position, it worsens with palpation.
- 53M + recent surgery + in hospital; Q asks for what post-surgical finding is most likely to reflect good recovery; answer = brisk diuresis; USMLE wants you to know that diuresis (urination) is a good sign of post-operative recovery. This is also the case in patients who have renal insufficiency who are being managed – i.e., brisk diuresis indicates recovery from the renal pathology.

- 40M + history of alcoholism + serum potassium of 3.2; following K⁺ administration, potassium remains at 3.2; why? → answer = hypomagnesemia; low Ca²⁺ and K⁺ non-responsive to supplementation → answer = check serum magnesium; Mg²⁺ required for basal level PTH secretion (↓ Mg → ↓ Ca); Mg²⁺ also inhibits a K⁺ secretory pump in the distal kidney (↓ Mg → ↑ K wasting); alcoholics are classic group at risk of hypomagnesemia due to mere dietary deficiency (EtOH is 7kcal/g, so they fill up on alcohol).
- 18M + gets lost hiking in woods for 3 weeks + BMI 27; what electrolyte are we worried about upon restoration of oral intake? → answer = hypophosphatemia; refeeding syndrome can cause various electrolytes to be low, but phosphate is the main one; mechanism is rapid sequestration of phosphate by glycolytic intermediates as glycolysis resumes.
- 31F + Hx of ITP + has splenectomy + platelet count goes back to normal; 6 months later, she has low platelets again; why? → answer = accessory spleen; 10% of people have a second, accessory spleen that is less than a centimeter in size; after splenectomy, the accessory spleen can grow in size; if the USMLE Q gives you ITP that was definitively managed with splenectomy, but then the ITP “comes back,” the answer is accessory spleen.
- 49M + long history of alcoholism + presents with smelly stools + pancreatic enzymes are normal; Dx? → answer = chronic pancreatitis → exocrine pancreas insufficiency due to repeated bouts of acute pancreatitis; pancreatic enzymes low or low-normal; steatorrhea from lack of lipases in pancreatic secretions; Tx with pancrelipase.
- 49M + alcoholism + had pancreatitis a week ago and recovered well with bedrest; now has fever + leukocytosis + increased serum lipase and amylase; diagnosis? → answer = pseudocyst; this is a common complication of acute pancreatitis; called a pseudocyst because it doesn’t have actual walls; the pancreatic parenchyma encases the fluid collection; can be drained internally via ERCP (2CK surg NBME).
- 40F + found in street with hypothermia + rewarmed in hospital + picture is shown of her feet and they’re red; what electrolyte are we most worried about? → answer = hyperkalemia → reperfusion injury causes oxygen radicals that increase the risk of rhabdo, especially in alcoholics.

- 82F + found in her house by the staircase; urine blood is 2+; RBCs on urine light microscopy are 3-4 per high-power field; diagnosis? → answer= rhabdomyolysis; classic finding is false-positive blood on urine dipstick; USMLE can give 3-4 RBCs/hpf as false-positive.
- 44M + recent surgery in hospital + tachycardia + fever + high BP; what drug should be administered? → answer = chlorthalidone; Dx is delirium tremens (alcohol withdrawal); Tx is benzo (diazepam, lorazepam, chlorthalidone). If the Q asks why tremulousness (tremor) present in delirium tremens, the answer is beta-2 agonism.
- 13F + asthma attack + tremor + albuterol + IV steroids given for acute asthma attack; why is there tremor? → answer = albuterol; tremor is most common side-effect of beta-2 agonists like albuterol.
- 57F + on various medications + comatose + seizure + prolonged QRS complexes on ECG; what med is responsible? → answer = amitriptyline; TCAs cause CCC → coma, convulsions, cardiotoxicity; ECG findings can be manifold; Tx with sodium bicarb (decreases binding of TCA to myocardial sodium channels; increased urinary excretion via alkalinization is wrong fucking answer and refers to NSAIDs; TCAs are basic, not acidic like salicylates).
- 22M + on anti-depressant med + has suprapubic mass + face is hot and red; which drug is he on? → answer = amitriptyline (any TCA is answer); TCAs also have nasty anti-cholinergic side-effects → *opposite of DUMBELSS* (refers to *cholinergic* side-effects) → diarrhea, urination, myosis, bradycardia, bronchoconstriction, excitation of skeletal muscle, lacrimation, salivation, sweating; so TCAs can cause constipation, urinary retention, mydriasis, tachycardia, bronchodilation (in theory, but this is more sympathetic beta-2-mediated, rather than anti-muscarinic), relaxation of skeletal muscle tone, dry eyes, dry mouth, anhidrosis (leading to heat retention and red, hot patient).
- 30F + going on a plane + receives diphenhydramine to prevent motion sickness; what receptor is responsible for anti-motion sickness in this patient? → answer = anti-muscarinic; diphenhydramine and chlorpheniramine are first-generation H1-blockers with nasty anti-cholinergic side-effects; muscarinic receptor blockade ameliorates feelings of motion sickness; H1 will not be listed as an answer in this case, so choose muscarinic; H2 might be listed, but diphenhydramine and chlorpheniramine don't act on H2.
- 24M + cuts his arm while scraping the BBQ in the backyard; which cell infiltrating into the area of the wound in the acute setting will most likely decrease his risk of a bacterial infection? → answer =

neutrophils; present in acute inflammation; part of innate immunity; phagocytose and kill bacteria via lysosomal hydrolases and H₂O₂ production.

- 55M + hyperthyroidism + pulses absent in left lower extremity; Dx? → answer = arterial embolic occlusion; acute limb ischemia in this case is caused by left atrial mural thrombus, secondary to hyperthyroidism-induced atrial fibrillation, launching off to the femoral artery; absence of pulses indicates arterial occlusion; in contrast, in DVT, pulses are **normal**, since the arteries are fine; AF can also lead to clot launching off to brain (stroke) or SMA/IMA (acute mesenteric ischemia).
- 80M + atrial fibrillation + severe abdominal pain + physical exam shows mild tenderness to palpation; Dx? → answer = acute mesenteric ischemia; pain out of proportion to physical exam is characteristic; left atrial mural thrombus from AF launched off to SMA or IMA.
- 65M + diabetes + Hx of CABG + intermittent claudication + pain in abdomen 1-2 hours after meals; most likely cause of abdominal pain? → answer = atherosclerosis; Dx is chronic mesenteric ischemia; presentation will sound like duodenal ulcer (pain 1-2 hours after meals) but in patient who has severe cardiovascular Hx. *H. pylori* causing duodenal ulcer, in contrast, will be a younger immigrant patient usually.
- 30M + rheumatoid arthritis + overdosed on methotrexate in suicide attempt + now has massive hepatonecrosis; the liver can regenerate via which of the following cellular mechanisms? → answer = recruitment of cells from G₀ into cell cycle; when there is hepatocellular damage, remaining cells in G₀ (quiescent phase) will enter G₁ of the cell cycle and begin replication; the wrong answer is stem cells entering G₁ of cell cycle; this is because stem cells aren't activated into G₁; it is merely the case that other hepatocytes exist in G₀, not undergoing replication, and are then stimulated into G₁ for replication.
- 500 factory workers are surveyed to determine whether they smoke or not and whether they have COPD or not; what kind of study design is this? → answer = cross-sectional survey; this is merely a snapshot of a population at one point in time; a survey group is called up, and then numbers of smokers vs non-smokers, and disease vs no disease, can be assessed. This determines prevalence of disease but not causation. This is different from case-control, where the initial study design is not that of calling up people and asking all of this info at once; instead, case-control entails taking two distinct

groups – one with COPD vs one without COPD, and then asking about their smoking history to attempt demonstrate causation.

- 20F + insulinoma; Q asks about C-peptide, insulin, and serum ketone levels; answer = ↑ C-peptide, ↑ insulin, ↓ ketones. C-peptide is a cleavage protein during the production of endogenous insulin, so if endogenous insulin is produced (i.e., via insulinoma), then C-peptide should be proportionally high. Ketogenesis is inhibited by insulin, so ketones must be low. Ketone production requires fatty acid breakdown into acetyl-CoAs as the starting blocks; beta-oxidation is inhibited by malonyl-CoA, which is an intermediate in fatty acid synthesis, as stimulated by insulin.
 - A tangential HY point is that DKA is not seen in type II diabetes because insulin is high initially; DKA is only seen in type I, since insulin is deficient. If a USMLE Q gives you acute type II diabetes and asks what's high in the patient's serum, the wrong answer is ketones; the correct answer is insulin (hyperinsulinemia due to insulin resistance).
- 2M + anemia + erythroblasts containing ferritin granules + enzyme analysis shows decreased delta-aminolevulinic acid synthase; administration of which vitamin might help this patient's condition? → answer = B6; diagnosis is X-linked sideroblastic anemia; first step of heme synthesis is succinyl-CoA + glycine, via delta-ALA synthase and vitamin B6, becomes delta-aminolevulinic acid; sideroblastic anemia is due to failure to synthesize delta-ALA and can be X-linked or classically caused by alcohol. Prussian blue staining of ringed sideroblasts is classic → iron cannot be incorporated into heme and remains within the RBC precursor around the mitochondria in a ring-distribution.
 - USMLE likes the heme synthesis disorders:
 - Acute intermittent porphyria → autosomal dominant; deficiency of porphobilinogen deaminase; buildup of porphobilinogen; Sx are abdominal pain, red urine, neuropathy. Tx w/ glucose and hematin can help.
 - Porphyria cutanea tarda → autosomal dominant; deficiency of uroporphobilinogen decarboxylase; buildup of uroporphyrins and coproporphyrins; Sx are photosensitivity and tea-colored urine.
- 62F + flank mass + serum calcium of 11.5 mg/dL + hemoglobin of 18.5 g/dL; diagnosis? → answer = paraneoplastic syndrome; renal cell carcinoma can produce PTHrp (correct, similar to SCC of the lung) and EPO (causing high hemoglobin). USMLE might give you a vignette of a smoker who has

hypercalcemia and polycythemia + show you a histologic specimen of many clear cells; clear cell carcinoma is the most common variant of RCC; USMLE likes you to know histo for RCC is clear cells. RCC can classically present with flank pain. Wilms tumor in a kid is painless flank mass.

- Neonate born at 28 weeks gestation + difficulty breathing; what is deficient in this patient? → answer = lamellar bodies; lamellar bodies are specialized organelles within type II pneumocytes that produce surfactant; dipalmitoylphosphatidylcholine (lecithin) / sphingomyelin ratio should be >2.0-2.4 for NRDS probability to be substantially decreased; elastic recoil is *increased* in NRDS due to lack of surfactant; surfactant normally prevents the hydrostatic forces of the alveoli from causing collapse.
- 30F + pancreatitis + ARDS; following complete resolution of the ARDS, what is most likely to be increased in this patient's lungs? → answer = surfactant protein D (marker of lung injury); weird, but know it because it's on NBME.



YouTube
@mehlmanmedical



Instagram
@mehlman_medical



MEHLMANMEDICAL HY INTERNAL MEDICINE

All material is copyrighted and the property of mehlmanmedical.

Copyright © [mehlmanmedical](http://mehlmanmedical.com)